A STUDY ON GASTRO INTESTINAL POLYPS

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DECLARATION

I solemnly declare that this dissertation "A study on Gastro Intestinal Polyps" was prepared by me in the Department of Medical Gastroenterology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3 under the guidance and supervision of Professor and HOD, Department of Medical Gastroenterology, Madras Medical College and Rajiv Gandhi Government General Hospital between December 2008 and January 2011.

This dissertation is submitted to the Tamil Nadu Dr.M.G.R.Medical University, Chennai-600 003 in partial fulfillment of the university requirements for the award of degree of DM Medical Gastroenterology.

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CERTIFICATE

This is to certify that the Dissertation entitled, **"A STUDY ON GASTROINTESTINAL POLYPS"** is the bonafide record work done by **Dr.Kani Shaikh Muhammad,** under our guidance and supervision in the Department of Medical Gastroenterology, Rajiv Gandhi Government General Hospital, Madras Medical College, Chennai, submitted as partial fulfillment for the requirements of D.M. Degree examination Branch IV MEDICAL GASTROENTEROLOGY, AUGUST 2011, under The Dr.M.G.R. Medical University, Chennai.

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CONTENTS

INTRODUCTION

The polyposis syndromes, a heterogeneous group of diseases, have been a major focus of study for the last decade and provide critical insight into the molecular pathogenesis of cancel'. Despite intense study, these important syndromes are still clinically confusing and proper objective identification is necessary for appropriate clinical management (Sweet et al., 2005).

The term "polyp" derives from the Greek for "multiple feet" or "little nipple". In current clinical practice a polyp is defined as any nodule or mass that projects above the level of the surrounding mucosa, as in the gut, to form a macroscopically visible structure (Najib et al., 2002; Vinay t'/ al., 2007). Traction on the mass may create a stalked, or pedunculated, polyp. Alternatively, the polyp may be sessile, without a definable stalk. The polyps that are formed as a result of abnormal mucosal maturation, inflammation, or architecture, are non-neoplastic and do not have malignant potential, but those that arise as the result of epithelial proliferation and dysplasia are termed adenomatous polyps or adenomas. They are true neoplastic lesions and

are precursors of carcinoma. Some polypoid lesions may be caused by submucosal or mural tumors. However, as with the stomach, the term polyp, unless otherwise specified, refers to lesions arising from the epithelium of the mucosa (Vinay et al., 2007).

Gastrointestinal polyps are being identified more frequently today because of increased awareness, screening and improved diagnostic tools. The entire gastrointestinal tract is at risk for polyp development but the adult colon and rectum account for the majority of polyps. Painless, bright red, rectal bleeding with normal stool frequency and consistency is the hallmark presentation of colorectal polyps at any age (Vinay et al, 2007; Attard and Young, 2006).

Gastric polyps are uncommon and are most frequently hyperplastic polyps, fundic gland polyps and adenomatous polyps. Hyperplastic and fundic gland polyps are essentially innocuous. In contrast, there is a definite risk of an adenomatous polyp harboring adenocarcinoma, which increases with polyp size (Vinayc/a/., 2007).

The classification of intestinal tumors is the same for the small and large bowel. Hyperplastic polyps are the most common polyps of the colon and rectum. When single, they do not have malignant potential. However a lesion known as sessile serrated adenoma, which has some similarities with hypeiplastic polyps, may have malignant potential (Vinay et al, 2007; Jass, 2003; Bariol et al., 2003; Snover et al., 2005, Torlakovic etal, 2003).

AIMS AND OBJECTIVES

To study the incidence and prevalence of gastrointestinal polyps with a clinical, endoscopic and histopathologic correlation.

REVIEW OF LITERATURE

Colorectal cancer is one of the most common neoplasms of industrialized nations, and accounts for approximately 9% of all cancer [1]. It is the second leading cause of cancer-related death in the Western world [2].

Most colorectal cancer develops from adenomas, the precursor lesions [2–5]. Adenomas are benignneoplasms with malignant potential; they may harbor an invasive carcinoma. Adenomas occur sporadically or as part of a polyposis syndrome. Hereditary polyposes account for approximately 1% of all colorectal carcinomas; hereditary non-polyposis colorectal cancer (HNPCC) accounts for approximately another 5%, and perhaps 30% or more of sporadic carcinomas may be inherited [6]. In addition to its clinical relevance as a precancerous lesion, the adenoma provides a model of early neoplastic change that has contributed to our understanding of the mechanisms of colorectal carcinogenesis [7]. Colorectal cancer is highly curable if diagnosed in the early stages [8], and malignant polyps constitute the precursors of early colorectal cancer. The pathologist plays a critical role in the management of the patient with endoscopically

removed polyps, especially malignant polyps, because the histopathological interpretation is the most important consideration for subsequent management [9].

ADENOMAS

Adenoma is a benign intraepithelial neoplasm composed of dysplastic cells. Most colorectal adenomas are present as protuberant masses or polyps. They must be differentiated from other types of epithelial polyps. They are classified according to the pathological process that is believed to underlie their origin [7]. Adenomas, the benign glandular neoplasms that precede colon cancer development, originate from the intestinal epithelium. They occur singly or in multiples. When multiple, the patients may have a genetic syndrome.

BIOLOGICAL ALTERATIONS IN ADENOMAS

Despite their differing structure, there are two common features in adenomas: a dysregulated proliferation and the failure to fully differentiate the epithelium. The dysregulated proliferation is evidenced by an upward shift in the proliferative compartment. Mitotic figures, including abnormal ones, are

present throughout the entire length of the hyperchromatic, adenomatous epithelium.

In the normal colon most apoptosis occurs near the luminal surface. Adenomas contain numerous apoptotic cells which often lie at the adenomatous base, a reversal of the normal distribution. This suggests that adenomas exhibit a reversed epithelial cell migration and have an inward growth pattern directed toward the crypt base rather than toward the lumen [10].

Adenomas also tend to show abnormalities in epithelial cell differentiation: adenomatous epithelium resembles the replicating cells normally present in the crypt base. Tall cells with prominent, elongated, hyperchromatic nuclei produce a characteristic “picket fence” pattern as they line the adenomatous glands. The adenomatous epithelium contains incompletely differentiated goblet cells and absorptive cells at all levels of the crypt, including the free surface. Adenomatous glands show no evidence of differentiation toward the luminal surface.

ADENOMA GROWTH

Small adenomas represent neoplastic clonal populations of colonic epithelial cells, suggesting that they arise from a single

abnormal precursor stem cell. Adenomas begin in a single crypt, and then grow by replacing normal epithelium in a centrifugal manner. Unicryptal adenomas are rare and most typically affect patients with adenomatous polyposis syndrome.

The neoplastic cells appear to cluster at the luminal aspect of the mucosa without extending to the base of the glands. Normal-appearing mucosa lies below the adenomatous glands. In 86% of early tubular adenomas, the number of glands opening along the polyp surface is larger than the number of gland bases; this difference increases with polyp size [11]. Gland proliferation is predominant in the upper crypts and along the surface of the lesions.

Early adenomas are present as small growths with a very benign tubular histology. The progression of most small adenomas is slow, and occurs over several years.

On average, small adenomas double their diameter in 10 years [12]. Some adenomas ultimately progress to invasive cancers, but not all adenomas progress; some may stay stable and may even regress or disappear while new ones may form [13].

INCIDENCE

Adenomas are the most commonly biopsied tumors of the large bowel [14]. Incidence rates of adenomas vary considerably throughout the world. Geographic areas exhibiting a high risk for colon cancer also exhibit a high risk for adenoma development, and vice versa. The incidence in the general population varies from 0% to 69%, depending on the country of origin [15,16] and on how the adenomas are detected [17]. In Western populations, the average prevalence rate for adenomas from flexible sigmoidoscopy screening is 10%, and colonoscopic screening prevalence averages 25% [18]. Adenomas accounted for 68% of all polyps removed by colonoscopy in the National Polyp Study [19].

In the 50- to 59-year age group, population screening studies and autopsy studies show an adenoma prevalence rate of 41.3% to 69% [20], increasing in advancing years up to 88% in centenarians [21]. Arminski and McLean [22] documented a 7.5% increase in adenoma incidence per decade.

Adenoma incidence peaks at age 60 to 70 years; it also occurs more frequently in men (61.6%) than in women (38.4%) [19].

Based on endoscopic studies, most sporadic adenomas arise in the rectosigmoid colon (66% to 77%) [23]. Adenomas also occur from a distal to a proximal location as patients age [15–17,24]; thus, left-sided adenomas are found more commonly in younger age groups, and right-sided lesions increase in frequency in individuals older than 65 years of age. Some adenomas tend to cluster. This means that multiple adenomas tend to occur closer together than would normally be expected from the general distribution of adenomas. This phenomenon occurs in all colonic segments, but is less pronounced in the rectum than in other parts of the large intestine [25].

MULTIPLE POLYPS

Individuals with one adenoma have a 40% to 55% likelihood of having additional synchronous lesions [23,26,27]. The additional adenomas can be detected at the same time as the initial adenoma (synchronous adenomas), or at a different time (metachronous adenomas). The prevalence of multiple adenomas

increases with age (about 9% of those under 60 years, and 28% of people older than 75 years have three or more adenomas). The incidence of large intestinal adenomas occurring synchronously with carcinomas is approximately double that of adenomas occurring alone.

A relationship exists between adenoma multiplicity and histological findings. In patients with a single adenoma, 38.8% are villous, whereas those with multiple adenomas have a 60.1% chance of having at least one villous adenoma [28]. Patients with multiple adenomas are also more likely to harbor at least one adenoma that contains high-grade dysplasia (13.8%) versus patients with a single adenoma (7.3%).

The overall recurrence rates for new adenomas are estimated from 20% up to 60%, with average followup times of 3 to 10 years after index polypectomy [17,23,29]. Most recurrences occur in the first two years following polypectomy. The estimated time of finding new adenomas is 58 months for patients clear on the first colonoscopy, and 16 months for patients who had adenomas on the first examination [30,31].

Villous tumors, particularly broadly sessile ones, usually have less well-defined borders than tubular adenomas, and therefore have a greater tendency to recur after local resection than smaller, pedunculated adenomas.

Endoscopic follow-up studies to evaluate new adenomas are hampered by the fact that as many as 25% to 27% of adenomas measuring less than 5 mm in diameter, and up to 6% of adenomas measuring 1 cm in diameter are missed during a single endoscopic examination [32,33]. Right-sided adenomas are missed more often (27%) than left-sided adenomas (21%) [32]. Relatives of individuals with colorectal cancer have an adenoma prevalence rate of 39%.

CLINICAL FEATURES

Bleeding is the most frequent symptom reported, and occurs more often in left-sided lesions than rightsided adenomas [34]. Small adenomas, ranging up to 1 cm in maximum diameter, usually remain asymptomatic unless they are traumatized by the passage of well-formed, hardened stool. Larger lesions become symptomatic, with the symptoms depending on polyp size and location. The bleeding is seldom severe. The incidence of bleeding

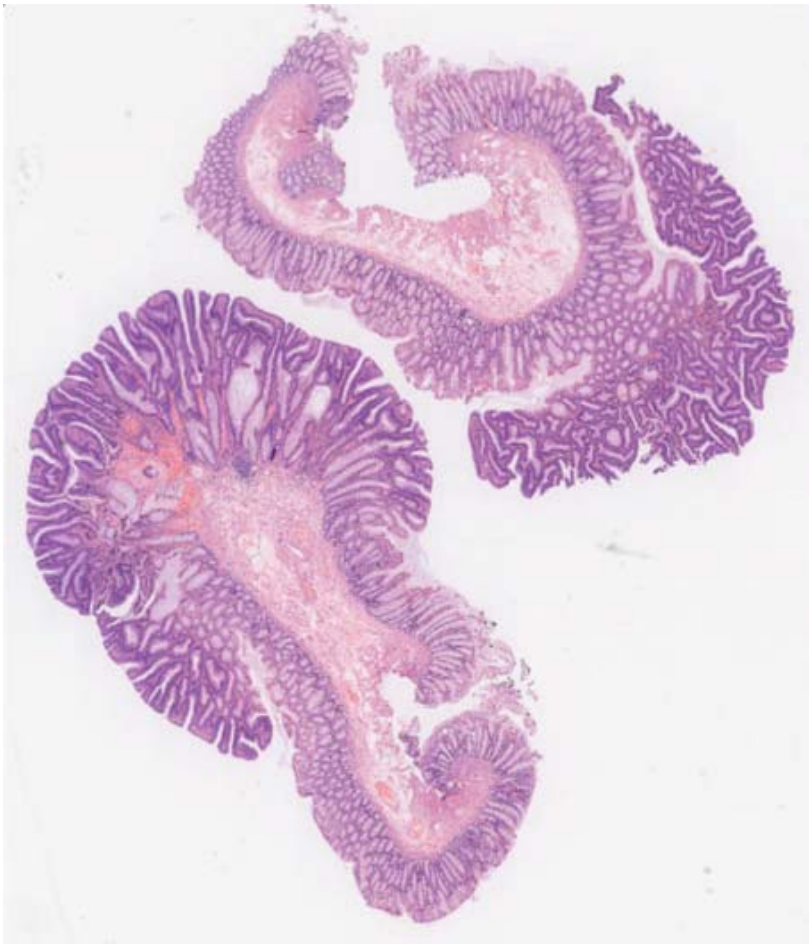
increases with increasing adenoma size and once a carcinoma develops within the adenoma. Villous tumors are more likely to bleed than tubular ones, since they tend to be larger [35]. Cecal lesions that block the appendiceal orifice may produce symptoms mimicking acute appendicitis.

GROSS FEATURES

Grossly, adenomas assume one of three major growth patterns: (a) pedunculated, (b) sessile, or (c) flat or depressed. Most sporadic colorectal adenomas appear as exophytic [8]. The categorization of adenomas according to their macroscopic appearance is important, as it may influence surgical treatment.

PEDUNCULATED ADENOMAS

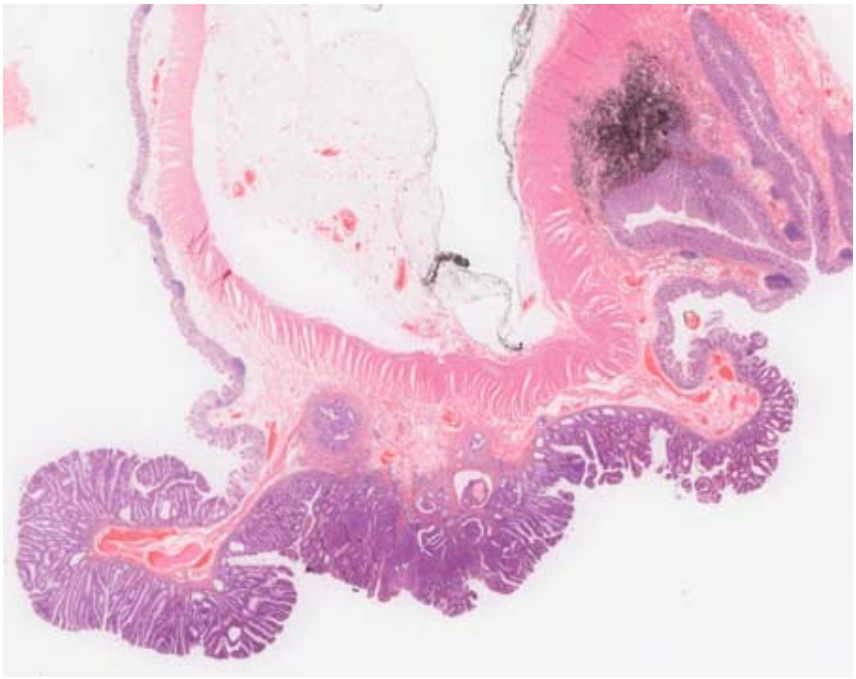
Pedunculated adenomas appear as exophytic, mucosal protrusions with a lobulated head and a stalk covered by normal mucosa. In pedunculated polyps, the adenomatous epithelium remains confined to the mucosa of the head of the polyp. The stalk consists of normal mucosa, including the muscularis mucosae and submucosal tissue, in continuity with the major part of the bowel wall.



Pedunculated polyp with the typical lobulated head and a stalk covered by normal mucosa

SESSILE ADENOMAS

Sessile adenomas attach to the mucosa by a broad base (Fig. 2.2). Sessile adenomas are often less well circumscribed than pedunculated ones. Because of their ill-defined edges, they are difficult to delineate, and have a greater tendency to recur following local excision.



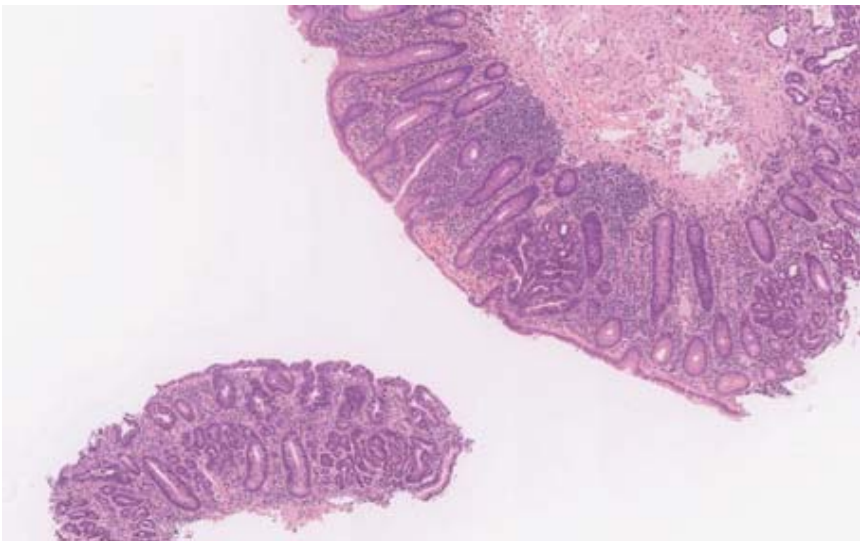
Sessile polyp attached to the mucosa by a broad base. On the right is a colonic tattoo: a collection of black non-degradable pigments in the submucosa

FLAT (DEPRESSED) ADENOMAS

The terms superficial, flat, and depressed non-polypoid adenoma are used synonymously to describe this entity [8], but have two different macroscopic aspects.

The overall prevalence of non-polypoid colorectal neoplasms is variable, and it accounts for from about 35% [36] to 42% of adenomas [37]. Flat adenomas are lesions that lack an exophytic polypoid configuration. They consist of slightly elevated dysplastic mucosal plaques that are never greater than

twice the thickness of the surrounding normal colonic mucosa [38] (Fig. 2.3). They constitute a special subgroup of adenomas with a greater potential for malignant transformation, while still being smaller than exophytic adenomas [8]. Depressed adenomas have a collarette of epithelium similar to that seen in a flat adenoma, but with a depression that is usually central. Because flat or depressed adenomas display little or no mucosal elevation,they can be very difficult to see endoscopically and pathologically, especially in the proximal colon [39]. They are often more clearly delineated endoscopically after spraying the mucosa with methylene blue or indigo carmine [40–43]. The failure to recognize these flat lesions may account for the lingering concept of de novo colorectal carcinoma [44]. Depressed adenomas tend to arise more commonly in the right colon than elsewhere [44]. They occur in HNPCC syndrome, sporadically, or in patients with familial adenomatous polyposis (FAP) [45]. The frequency of flat adenoma is 50.7% in HNPCC patients. Generally, adenomas appear as grossly homogeneous, soft lesions without induration, ulceration, or fixation. Areas of ulceration, depression, or firmness suggest the possibility of a coexisting carcinoma.



Flat adenoma: low-power photomicrograph demonstrating a flat adenoma with approximately the same thickness of non-neoplastic colonic mucosa and containing crowded glands lined by hyperchromatic and mucin-depleted epithelium concentrated at the surface. In the biopsy on the right there are non-neoplastic glands on each side of the dysplastic epithelium

HISTOLOGICAL FEATURES

There are four categories of adenoma: tubular, villous, tubulo-villous and flat-depressed [8]. The factors controlling the growth pattern of adenomas are unknown [7].

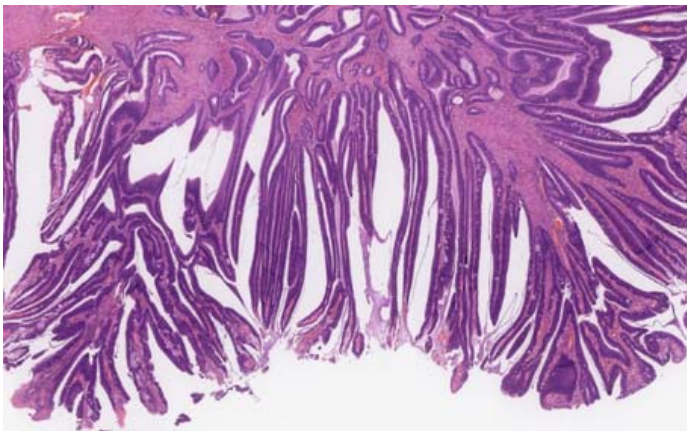
TUBULAR ADENOMA

Tubular adenomas maintain the original crypt architecture, but adenomatous epithelium replaces the normal colonic epithelium in lining the crypts (Fig. 2.4). This is the most common type of adenoma (about 68% to 87%) [19,46,47]. Tubular lesions are those that contain greater than 80% of a tubular component.

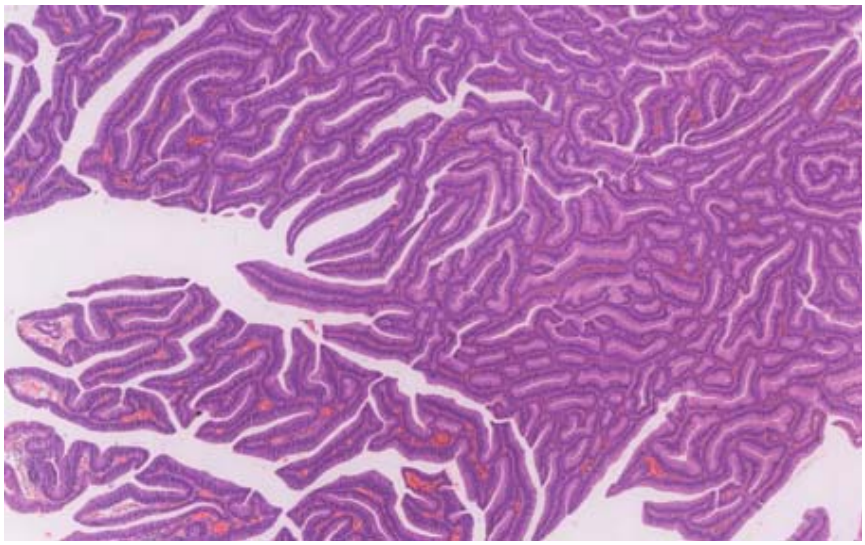
Tubular adenomas consist of closely packed branching tubules separated by varying amounts of lamina propria. The tubule may be relatively regular, or when the adenomatous tubules grow, they may branch and show considerable irregularity. Small tubular adenomas usually have a dysplastic surface epithelium overlying normal epithelium in the crypt base.

VILLOUS ADENOMA

Villous adenomas (approximately 20%) have villi with cores of lamina propria covered by a single layer of adenomatous epithelium. Villous lesions are those that contain greater than 80% of a villous component [46] (Fig. 2.5). Villous adenomas fall into three types: (a) flat, carpet-like masses; (b) lobulated, bulky, sessile masses; (c) pedunculated lesions with short, broad pedicles.



Villous adenoma characterized by long finger-like fronds lined by neoplastic epithelium



Tubulo-villous adenoma: mixture of tubular and villous architecture – villous fronds and tubular glands

TUBULO-VILLOUS ADENOMA

Tubulo-villous adenomas contain a mixture of both tubular and villous patterns, or have broad villi containing short tubular structures. Tubulo-villous lesions are those that contain from 20% to 79% villous components [46]. They tend to be larger than tubular adenomas, with a mean diameter of 19 mm [22] (Fig. 2.6). A villous component is present in 35% to 75% of all adenomas measuring more than 1 cm in largest diameter [48].

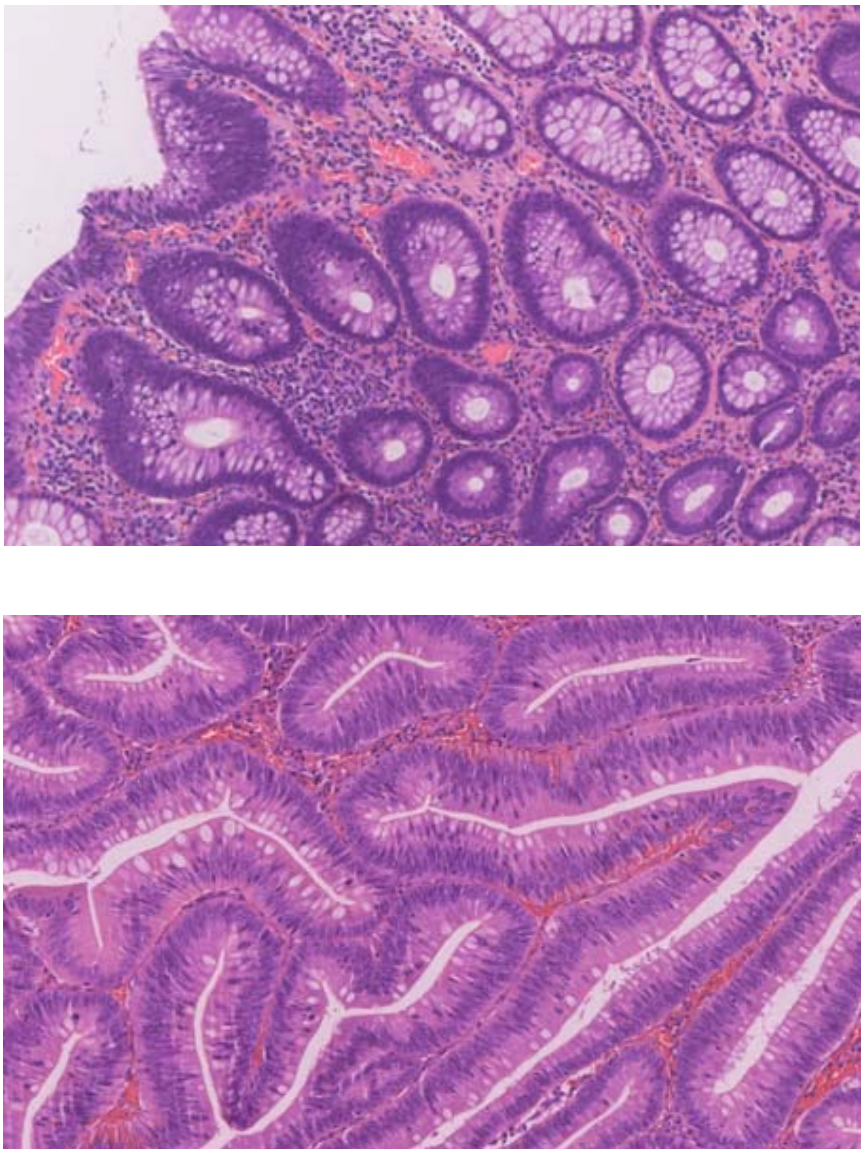
FLAT-DEPRESSED ADENOMA

Flat or depressed adenomas are a variant of tubular adenoma with little or no mucosal elevation. The thickness of the adenomatous mucosa does not exceed twice than that of the

normal mucosa [8], and the adenomatous changes concentrate near the luminal surface. Flat adenomas have a high incidence of highgrade dysplasia [38,45], and they are more likely to harbor invasive carcinoma than is typically seen in polypoid counterparts [49]. There is a high association with synchronous and metachronous invasive colorectal carcinomas [8]. Depressed adenomas measuring less than 1 mm in diameter show horizontal growth between the normal adjacent crypts, often leaving normal crypts entrapped as residual islands.

DIAGNOSIS

The histological features of adenomas may be defined as low- or high-grade dysplasia. 2.10.1 Low-Grade Dysplasia Low-grade dysplasia consists of stratified dysplastic epithelium that retains its columnar shape. The nuclei are spindle or oval shaped. The stratified nuclei tend to remain in the basal epithelium, extending no more than three-quarters of the height of the epithelium. Minor cytological variations including numerous mitoses, mild nuclear pleomorphisms, and variations in cell size and shape may occur in adenomatous epithelium; however, these features (more common in larger polyps) are insufficient for a diagnosis of high-grade dysplasia.



Low-grade dysplasia; a, small tubular adenomatous gland with very little atypia; normal colonic glands on the right; b, small tubular adenomatous gland with moderate atypia

Sometimes it is difficult distinguish a small tubular adenoma from reactive epithelium present in an inflamed mucosa, because reactive glands appear more basophilic than normal and the nuclei may exhibit pseudostratification. In these cases it is useful

examine the degree of differentiation of the epithelium along the length of the tubular crypt. If the entire gland is not replaced by basophilic epithelium, then its restriction to the bottom portion of the crypt serves to identify the epithelium as regenerative. Conversely, in small adenomas, the adenomatous glands appear more basophilic at the surface of the lesion, and nonneoplastic epithelium lies below it [8].

HIGH-GRADE DYSPLASIA

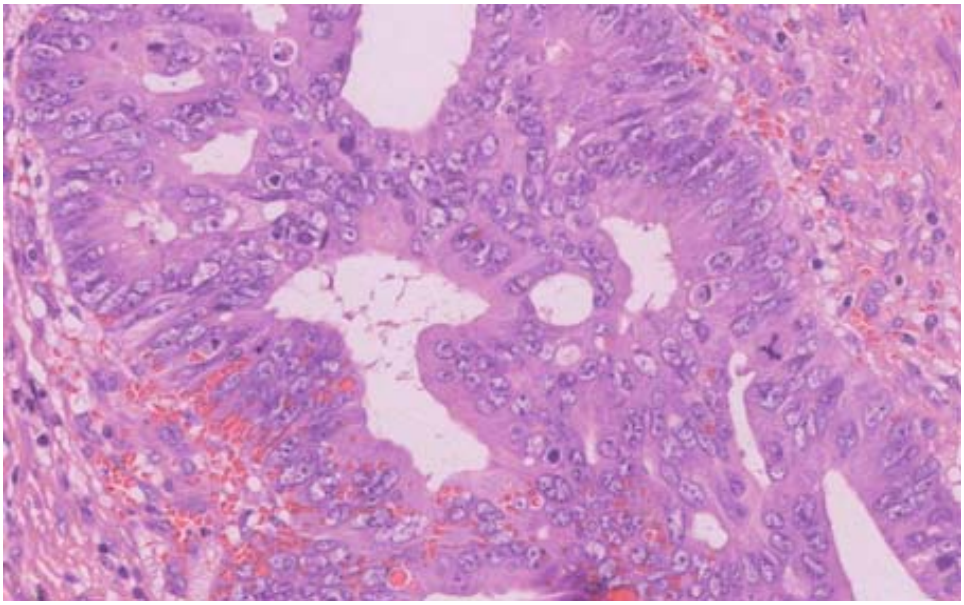
High-grade dysplasia is characterized by the presence of marked cytological atypia, the loss of cellular polarity, stratification of cells to the luminal surface of the glands, and crowding with occasional formation of solid nests of dysplastic cells. The cells show loss of columnar shape with cellular rounding and an increase of nuclear-to-cytoplasmic ratios. Cells remain confined within the basement membrane of the original colonic crypt, or they may extend into the surrounding lamina propria, with a cribriform pattern obliterating the intervening stroma. Glandular density increases. (Fig. 2.8b) The presence of high-grade dysplasia strongly correlates with a contiguous invasive carcinoma.

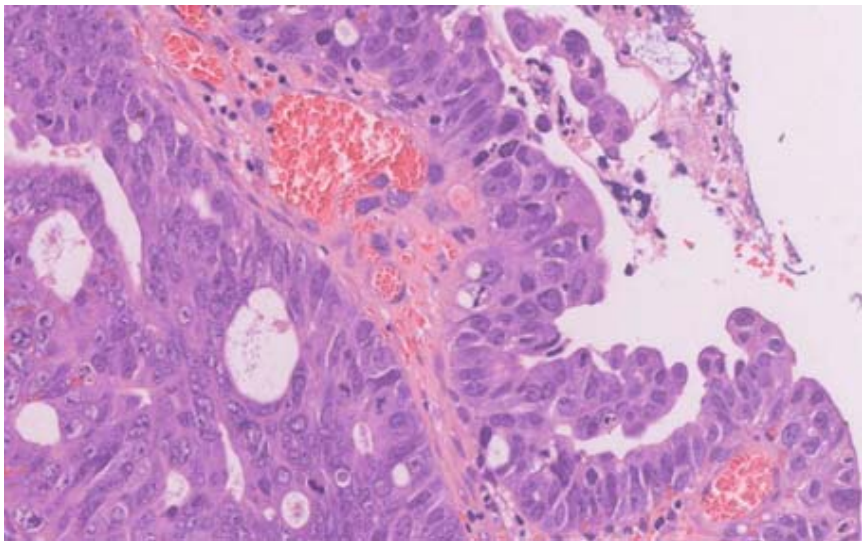
High-grade dysplasia represents the extreme end of the spectrum of abnormal histological changes, short of invasive carcinoma in the adenoma–carcinoma continuum. Individual adenomas may contain transitions between high-grade and low-grade dysplasia. The percentage of adenomas containing high-grade dysplasia increases significantly with increasing adenoma size, villous architecture, multiplicity of adenomas, and age greater than 60 years [50,51]. High-grade dysplasia encompasses the histological changes called carcinoma in situ [9] and intramucosal carcinoma (Fig. 2.8a). The latter is when there is extension of the neoplastic cells through the basement membrane of the crypt into the surrounding lamina propria but not beyond [52,53]; intramucosal carcinoma includes that which involves the muscularis mucosae. Neoplastic glands in and among a splayed muscularis mucosae is not invasive cancer. Only when cancer invades into the submucosa does it have the potential to metastasize [8,9,52].

Neither carcinoma in situ nor intramucosal carcinoma have a clinically significant potential for metastasis (if all neoplastic tissue is removed), and the lesions do not require additional

treatment [8]. Hence this term should only be used in conjunction with the comment that intramucosal adenocarcinoma lacks the potential for metastases, and if totally removed it has been adequately treated [9].

The pathology report should state the macroscopic description (pedunculated or sessile polyp, and the greatest dimension), the highest degree of dysplasia present in the adenoma, whether or not it has villous features, the completeness of its removal, and the presence or absence of invasive tumor [54].





High-grade dysplasia; a, characterized by cellular disorganization and more marked cytologic atypia, the degree of nuclear pleomorphism is sufficient to call it intramucosal carcinoma; b, stratification of cells to the luminal surface of the glands, a feature of high-grade dysplasia

REPORTING COLORECTAL ADENOMA

Gross features

- Macroscopic growth pattern: pedunculated/sessile/ flat polyp.

- Greatest dimension.

Histological features

- Architecture: tubular/villous/tubulo-villous.

- Grade: low-grade/high-grade dysplasia.

- Status of the resection margin.

ADENOMA–CARCINOMA SEQUENCE

Adenoma constitutes the precursor lesion for most colorectal carcinomas [2–5]. Two concepts can explain the understanding that now exists in relation to the evolution of colorectal neoplasia. The first is the model provided by the adenoma–carcinoma concept and is supported by clinical, pathological, and epidemiological data collated over several decades [3]. The second model is related to the hereditary bowel cancer syndromes (FAP and HNPCC) that led to the discovery of important cancer genes [55,56].

The earliest lesions consist of pseudostratified, immature, mildly dysplastic, adenomatous cells. In some cases, one may see a continuous histological spectrum of increasing degrees of dysplasia culminating in the development of an invasive carcinoma [8].

There are publications purporting “de novo” carcinomas that are open to various interpretations. It should be recalled that adenomas may, on rare occasions, be flat or even depressed, presenting essentially as dysplasia within flat mucosa [40,57]. “De novo” carcinoma may represent an early cancer that has destroyed

a small adenoma [58]. Nevertheless, some studies support the view that the “de novo” cancer and classical cancer represent divergent evolutionary pathways. “De novo” carcinoma shows a non-polypoid, superficially spreading, growth pattern, and a more aggressive course [7].

Morphological features that determine the malignant potential of an adenoma are size, growth pattern, and grade of dysplasia [7]. Carcinomas are more likely to arise in larger adenomas than smaller ones. The incidence of carcinoma in an adenoma increases as the size of the adenoma increases. The prevalence of cancer in adenomas under 1 cm is only about 1%, in those between 1 and 2 cm in diameter it is about 10%, and in those over 2 cm there is nearly a 50% malignancy rate.

Adenomas with a villous pattern have a higher malignant potential than those with a tubular pattern.

The malignancy rate for tubular adenomas is about 5%, but rises to 40% in villous ones. In tubulo-villous types, the malignancy rate is about 22%. Although histological type is very important in the assessment of malignant potential, it seems that size is the paramount feature [59].

The malignant potential of an adenoma increases as grading of dysplasia increases, irrespective of histological growth pattern. Both growth pattern and dysplasia grade correlate with adenomatous size. Usually, small adenomas (those under 1 cm) show low-grade dysplasia and have very low malignant potential. The risk of cancer developing in such adenomas is only 5% after 15 years. The malignancy rate rises to 27% if a high-grade dysplasia is present; however, it is rare in a polyp of this size. A similar relationship is seen in adenomas that are 1 to 2 cm in diameter in relation to the grade of dysplasia. In adenomas over 2 cm in size, the malignancy rate is high but bears little relation to the degree of dysplasia.

Although the trend observed for size and malignant change is considerably greater than the trend for dysplasia and malignancy, there are reasons to suspect that at the biological level of dysplasia is the most selective marker of increased malignant potential [7]. Even though adenomas clearly constitute the precursor lesion for most carcinomas, a vast gap exists in the prevalence rates of adenomas and carcinomas, indicating that

some 90% to 95% of adenomas will never become malignant during a person's lifetime [16].

This fact offers the challenge of developing markers for the identification of those adenomas that have a high probability of progressing to an invasive carcinoma.

Actuarial analysis reveals a cumulative risk of developing cancer in adenomas that are not removed at 5, 10, and 20 years of 2.5%, 8%, and 24%, respectively. It is estimated that the conversion rate of adenomas to cancer is 0.25% per year [60].

ADENOMAS CONTAINING CARCINOMA (MALIGNANT POLYPS)

A malignant polyp is an adenoma containing invasive carcinoma. The diagnosis of invasive carcinoma is made when neoplastic glands have invaded and penetrated through the muscularis mucosae into the submucosa of the bowel wall or into the submucosa of the stalk of an adenoma [9,61]. Invasio into, but not through, the muscularis mucosae is still "intramucosal carcinoma". Desmoplasia often surrounds the invading glands, which have irregular, angled contours and show cytological

features of malignancy [8]. This feature must be differentiated from “entrapped” (pseudoinvasive) mucosa.

Submucosal invasion is most easily recognized by the intermingling of the malignant glands with normal submucosal structures including medium-sized blood vessels, fat, nerves, ganglia, and large lymphatics [8]. Various degrees of substitution of an adenoma by carcinoma may occur. A polypoid carcinoma is a polyp consisting entirely of cancer with no remaining benign adenoma.

Malignant adenomas represent an early form of colorectal carcinoma. Approximately 42 to 85% of early colorectal cancers are pedunculated, and 15–58% are sessile [62,63]. Carcinomas arising from pedunculated adenomas cause the biggest clinical questions with regard to further management. Various opinions exist for managing patients after endoscopic removal of malignant polyps. Some of these lesions require further therapy, others do not.

One possibility is that all patients with malignant polyps should undergo standard resection [64]; another opinion is that a conservative approach should be maintained in the absence of

cancer at the resection line [65]. The present mainstream opinion, however, is that all malignant polyps removed by endoscopic polypectomy require evaluation of histological parameters that have been demonstrated to be significant prognostic factors related to the risk of adverse outcome (i.e. lymph node metastases or local recurrence from residual malignancy) after polypectomy [54,65–69]. The management of these malignant adenomas depends upon their histological risk factors and the patient's general condition [70].

The dilemma about managing patients after endoscopic removal of malignant polyps is best resolved by a multidisciplinary team involving the surgeon, pathologist, and endoscopist, and taking the patient's condition and wishes into account [70]. The clinician faces the therapeutic decision as to whether or not polypectomy alone is adequate therapy or whether the patient requires a definitive surgical resection; therefore, the metastatic risk must be determined to plan future therapy.

After endoscopic polypectomy, all the histological risk factors need to be simultaneously and carefully evaluated by the pathologist to identify and classify patients into low-risk or a

high-risk group associated with an adverse outcome (i.e. lymph node metastasis or local recurrence from residual malignancy) [68,71].

PROGNOSTIC FACTORS OF METASTATIC

Risk or Residual Disease Present in Malignant Adenomas Histological parameters have been developed over the years to identify prognostic factors of metastatic risk and reduce the number of unnecessary additional laparotomies, while selecting which adenomas have very little or virtually no risk of nodal metastasis and/or local recurrence [68].

The pathological features that have independent prognostic significance and that are crucial for evaluating risk of adverse outcome (e.g. increased risk of residual disease or lymph node metastases) include histological grade, completeness of resection margin, lymphatic-venous vessel involvement, tumor budding, and level of invasion of the submucosa.

GRADE OF DIFFERENTIATION

The grading system is based on gland or tubule formation and the cytological features of adenocarcinoma (how closely it approximates normal epithelium) [9]. The neoplastic components

should be divided into well-differentiated (grade 1 – G1), moderately differentiated (grade 2 – G2), poorly differentiated adenocarcinoma (grade 3 – G3), and undifferentiated carcinomas (grade 4 – G4). The World Health Organization (WHO) classifies the neoplastic components into just two categories: low-grade (G1 and G2) and high-grade (G3 and G4) adenocarcinomas [61]. Well-differentiated (G1) adenocarcinoma exhibits glandular structures in more than 95% of the tumor. Moderately differentiated (G2) adenocarcinoma has 50 to 95% glandular structure. Poorly differentiated (G3) adenocarcinoma has 5 to 50% glandular structure. Undifferentiated (G4) carcinoma has less than 5% glandular structure [61]. In order to reduce the degree of inter-observer variability in the grading of adenocarcinoma, and in light of its prognostic value and relative simplicity and reproducibility, a two-tiered grading system for colorectal carcinoma has been recommended: low-grade carcinoma (gland formation greater than or equal to 50%) and high-grade carcinoma (gland formation less than 50%) [72]. The histological grade is assigned according to the least-differentiated area found, even though this may appear to be quantitatively insignificant [8]. Tumor grade is classified as a

favorable grade (low-grade adenocarcinoma) or an unfavorable grade (high-grade adenocarcinoma) [68].

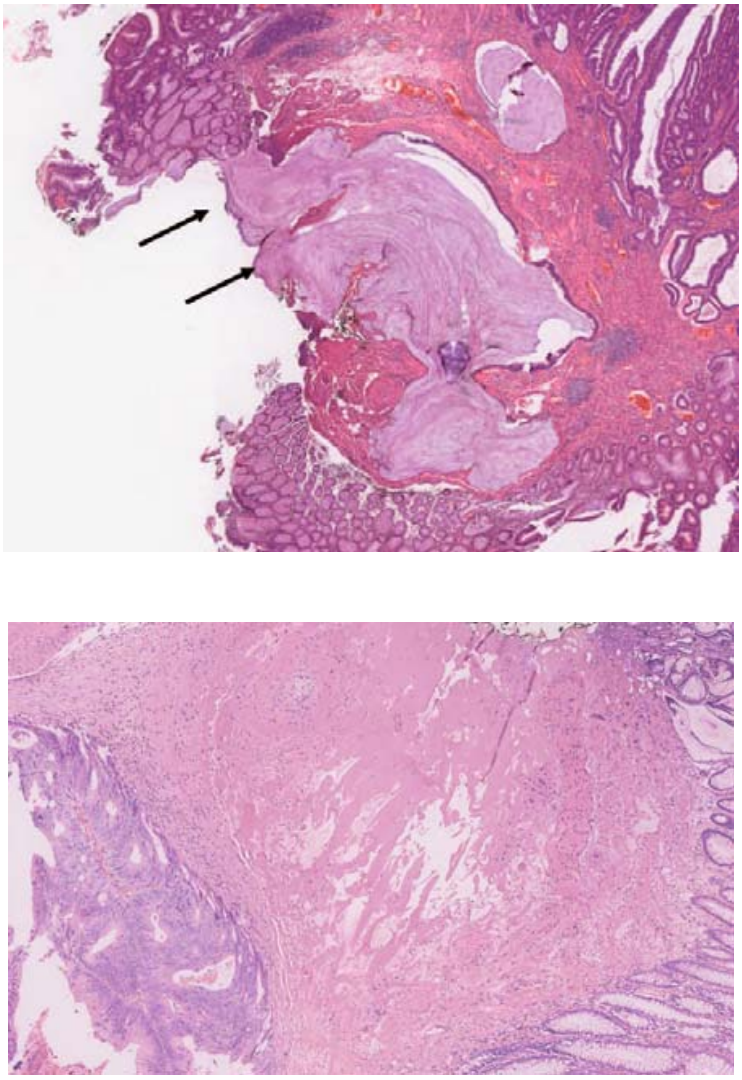
MARGINS

The margin of resection, or transection point, is defined as the actual free edge of the submucosal connective tissue that contains diathermy change [9]. A tumor at the margin is defined as cancer cells extending up to the actual transected soft tissue margin. A tumor near the margin is defined as cancer cells less than or equal to 1 mm from the transected margins, cancer within the diathermy change, or within one high-power field of the cautery effect [9]. The presence of a tumor at or near the resection margin has the same clinical significance and is associated with intramural recurrence after local excision an adverse outcome [9], even in the absence of any other unfavorable parameters [8].

LYMPHATIC INVASION

The diagnosis of lymphatic invasion requires the presence of cancer cells within endothelium-lined channels [9] (Fig. 2.10). Lymphatic invasion may be confused with retraction artifact. These are most commonly encountered within the invasive tumor itself, rather than in the submucosa away from and surrounding the

actual invasive cancer [73]. The retraction artifact is often seen around small clusters of tumor cells, where reactive fibroblasts often surround tumor cells and mimic endothelium-lined channels.



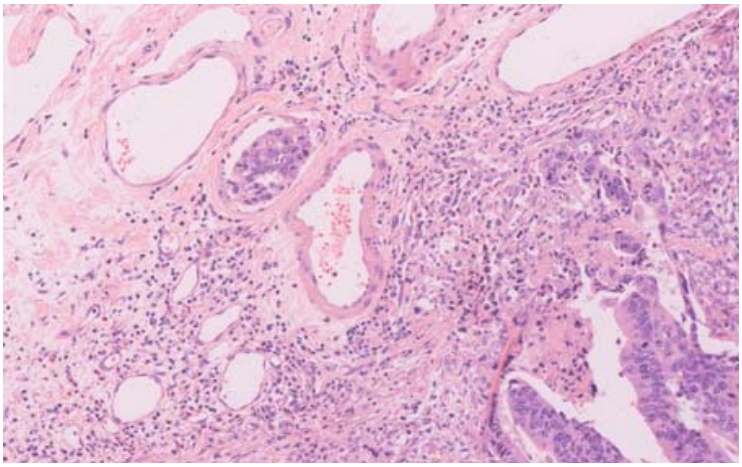
Malignant polyps; a, with cancer at the resection margin, arrows indicate resection margin; b, with cancer near (1 mm) the resection margin (diathermy effect is evident on the right)

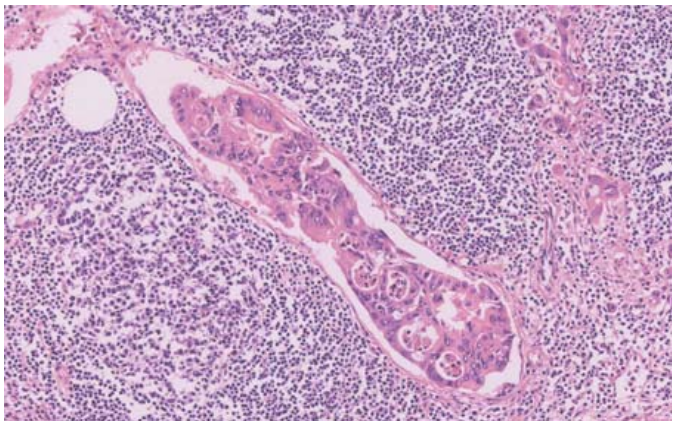
When questionable areas for lymphatic invasion are present, subsequent serial and deeper sections are recommended [9]. Immunohistochemistry studies have not been of great help in establishing or excluding lymphatic invasion [9].

VENOUS INVASION

Venous invasion is defined as tumor emboli within endothelium-lined channels surrounded by a smooth muscle wall. When one suspects venous invasion, multiple serial or deeper sections (and possible elastic stains) are quite helpful in deciding whether venous invasion is present [9].

The degree of lymphovascular invasion has been defined by the Japanese Society for Cancer of the Colon and Rectum. Lymphatic (ly) or vascular (v) invasion may be absent (ly0, v0), slight (ly1, v1), moderate (ly2, v2), or massive (ly3, v3) [62].





Lymphatic invasion encountered in the submucosa (a, magnification 20×; b, magnification 30×)

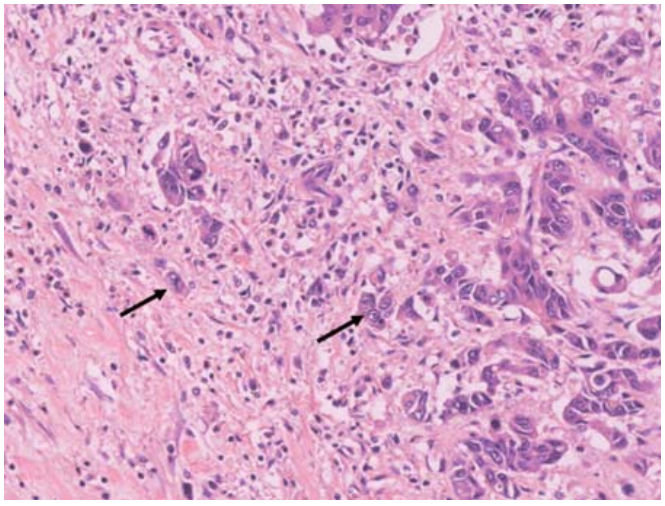
TUMOR BUDDING

Tumor budding, also known as dedifferentiation, is a recently recognized feature that represents a highgrade, undifferentiated component of a tumor at the leading invasive edge [74] (Fig. 2.11). It is defined as an isolated single cancer cell or a cluster composed of fewer than five cancer cells observed in the stroma of an invasive frontal region [75]. A budding count must be done after choosing one field where budding is the most intensive. in a field measuring 0.785 mm2, using a 20× objective lens [69]. A field with fewer than five budding foci is viewed as negative [76]; one with five or more buds is viewed as positive [68].

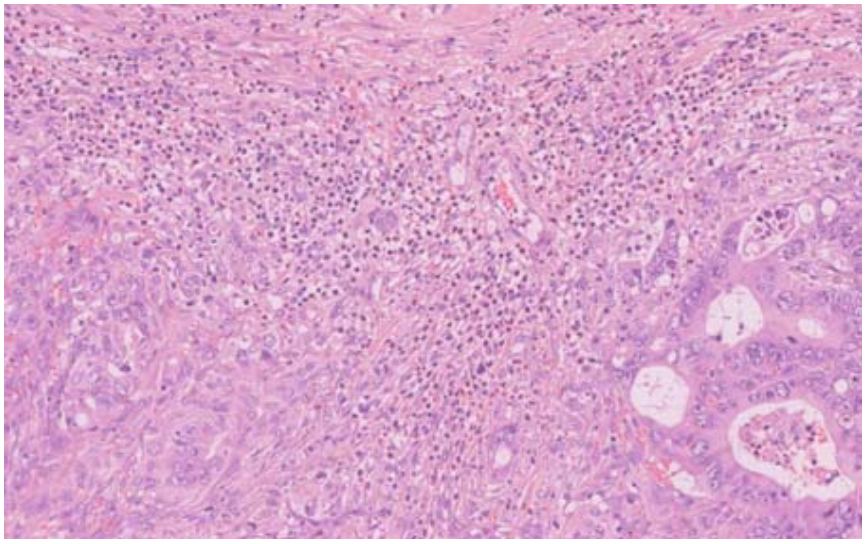
Nonetheless, the intensity of tumor budding also seems to be important [77]. Recent evidence suggests that tumor budding is associated with both lymphatic invasion and nodal metastases [75,78,79]. A number of 0 to 9 foci are classified as a low-grade or low- “intensity” tumor budding, while 10 or more buds are a high-grade or high-“intensity” tumor budding [79]. Higher intensity of tumor budding is significantly associated with higher risk of postoperative recurrence [80]. The disease-free survival and the overall survival rates dramatically decrease in patients with an intensity greater than nine tumor buds [80]. Intensity greater than nine may be considered to be an adverse prognostic indicator in patients with colon carcinoma [80].

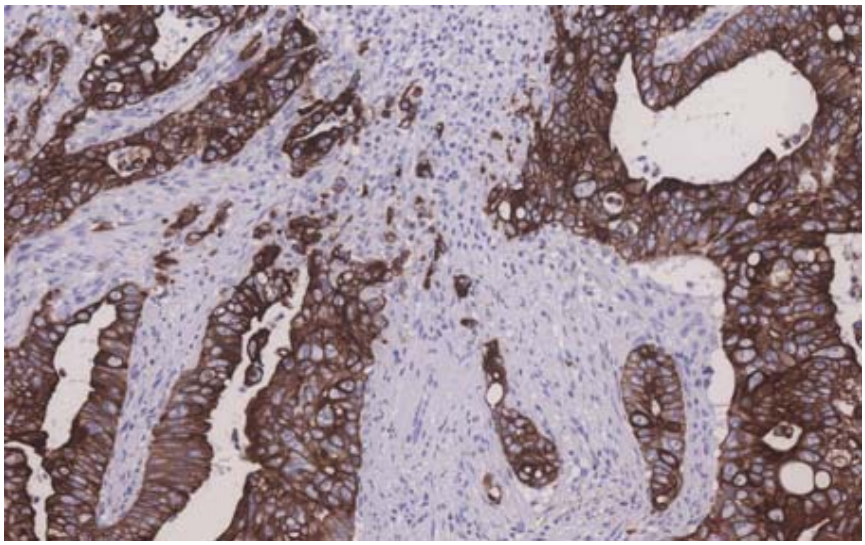
Because cell clusters (buds) at the leading invasive edge may be quite small and do not form glands or produce mucin, identification on histopathological examination may be difficult [74] (Fig. 2.12a). A pancytokeratin immunostain may be helpful in their identification, especially if accompanied by an inflammatory reaction that obscures their presence on hematoxylin- eosin stain [74,80] (Fig. 12b).

Results indicate that tumour budding is a useful risk factor for predicting lymph node metastases in cases of early colorectal cancer [81].



Early colorectal cancer with high degree of tumor budding: isolated single cancer cell or a cluster composed of fewer than five cancer cells is defined as a budding focus. Arrows, budding foci





Colorectal cancer. a, early colorectal cancer with low degree of tumor budding. The identification of budding foci is difficult because the buds are obscured by inflammatory reaction (magnification 12×); b, tumor budding highlighted by immunohistochemistry: by using a pan-cytokeratin antibody, budding is easily seen (magnification 20×)

ADENOCARCINOMA IN THE SUBMUCOSA (MICROSTAGING)

If invasive cancer is present, it should be reported the amount of adenocarcinomatous component in terms of the volume of adenoma replaced by the carcinoma, the depth of its invasion, and the width of horizontal spread in the submucosa. This process can be called microstaging, and allows the ability to report both the level and the extent of the infiltration into the submucosal layer.

VOLUME OF ADENOMA REPLACED BY THE CARCINOMA

The volume of adenoma replaced by the carcinoma can be measured. This is a quantitative ratio, expressed as a percentage. Lesions with small foci of invasive carcinoma have lower metastatic capability than polyps that are mostly made of invasive carcinoma [82].

DEPTH OR LEVEL OF INVASION OF THE SUBMUCOSA

Different staging of invasion into the submucosa has been proposed for pedunculated and sessile polyps. The Haggitt levels are used for carcinoma in pedunculated polyps [53], and the Kikuchi levels [64] are used for carcinoma in sessile polyps [62].

The level of invasion in a pedunculated malignant polyp is defined within four levels:

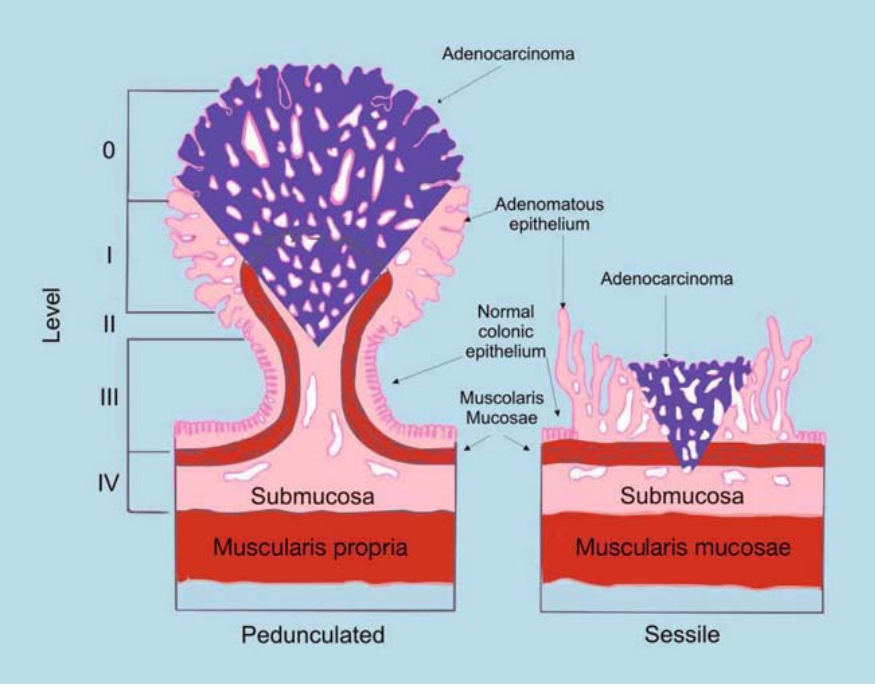
- Level I: invasion is limited to the head of the polyp
- Level II: invasion into the junction of head and stalk
- Level III: invasion into the stalk.
- Level IV: invasion in the submucosa below the stalk.

The level of submucosal (sm) invasion in sessile malignant polyp is defined within three levels:

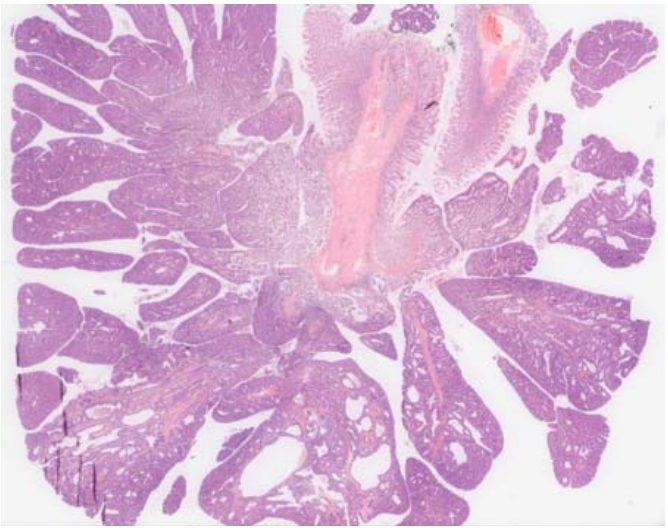
- Sm1: slight submucosal invasion from the muscularis mucosae to the depth of 200–300 μm
- Sm2: intermediate invasion.
- Sm3: carcinoma invasion near the inner surface of the muscularis propria.

Considering polyp morphology, the sessile type is associated with a unfavorable outcome as compared with that of pedunculated type. Although patients with sessile polyps frequently underwent surgery (85%) [83], their overall mortality remained roughly eight times higher when compared with patients with pedunculated polyps. This seems to be mainly due to a significantly higher prevalence of all the histological risk factors in this group rather than to a predetermined biologically aggressive behaviour [84,85]. In detail, a positive resection margin seemed to be by far the most crucial risk factor in sessile polyps, probably because of an inadequate endoscopic removal of these lesions.

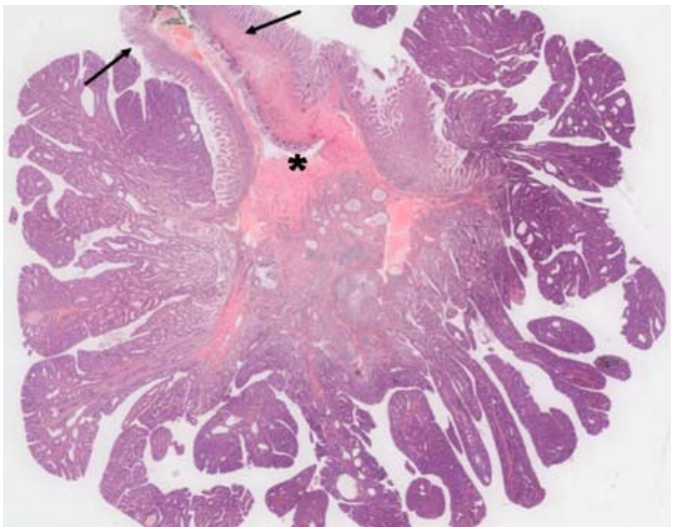
This confirms the previous analysis by Haggitt et al [53], in which the level of invasion, but not the sessile morphology, seemed to be an independent risk factor for an adverse outcome [83].



Haggitt's levels. Modified from [53], with permission from Elsevier



Pedunculated early colorectal cancer: Haggitt's level I with invasion limited to the head of the polyp

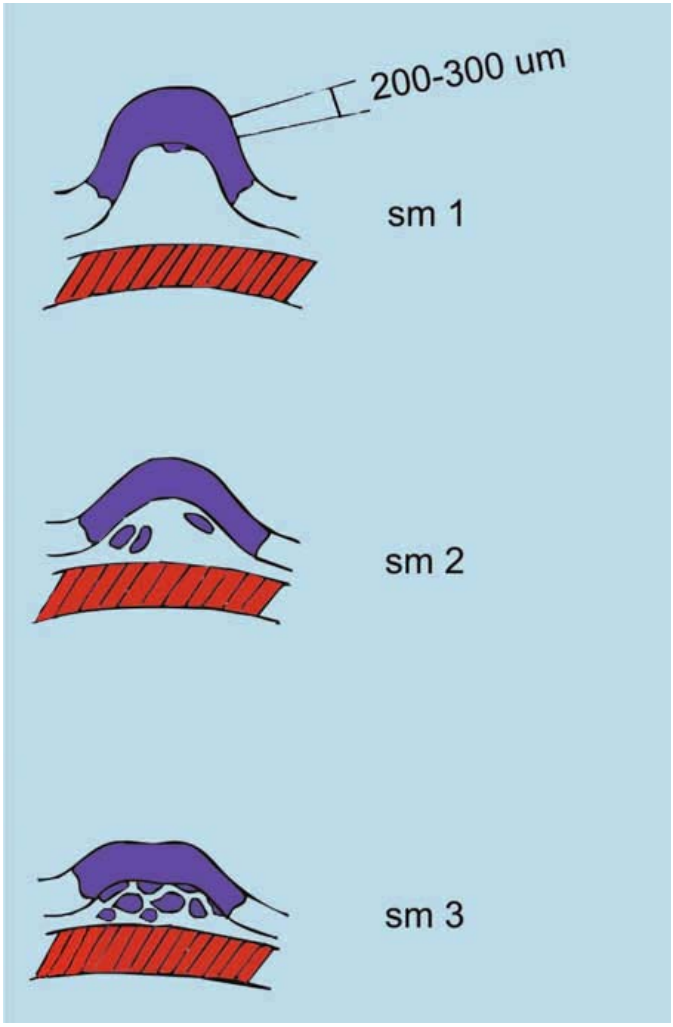


Early colorectal cancer: Haggitt's level II (invasion to the junction of head and stalk). The margin is the cauterized submucosa (black star) and not the dangling wings of mucosa (arrows)

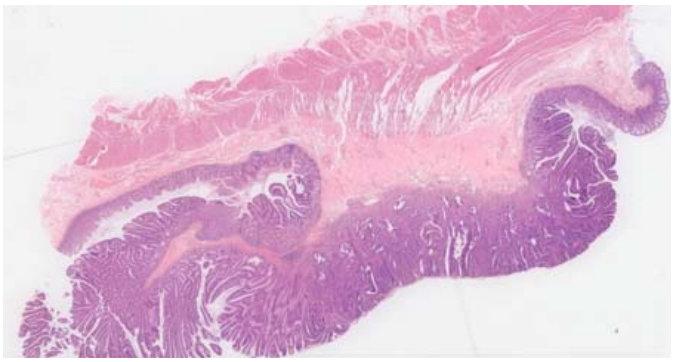
The Haggitt classification is less useful for sessile tumors. According to these criteria, invasive cancer arising in a pedunculated adenoma could be classified as level I to level IV. Invasive cancer arising in a sessile adenoma is, by definition, a level IV lesion (Fig. 2.17). In sessile and semi-sessile adenomas there will most likely be an invasion into the submucosa of the bowel wall, and the patient will therefore be at higher risk for metastasis compared to early invasive carcinomas arising in pedunculated adenomas [8].

MEASURING THE LEVEL OF SUBMUCOSAL INVASION

Extension into the submucosal layer may be expressed by micrometric measurement of depth and width of submucosal invasion. It is a numerical measurement regarding depth and width of tumor invasion. Depth invasion (vertical distance) is estimated from the lower edge of the muscularis mucosae to the deepest invasive front. When the muscularis mucosae cannot be identified, the vertical distance from apex of the tumor to the deepest invasive front is measured. Width invasion measures the greatest width of submucosal of invasion [68].



Kikuchi's levels. Modified from [63]



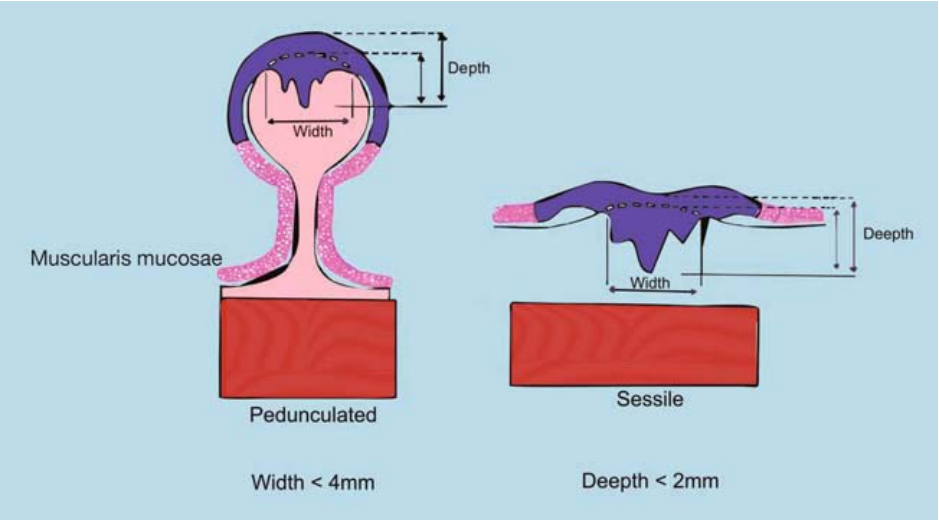
Sessile early colorectal cancer: Haggitt's level IV; Kikuchi's level sm1 with invasion from the muscularis mucosae measuring less than 300 µm deep

Numerical data regarding the extent of submucosal invasion aids in identifying tumors with very little risk for nodal involvement in patients with an absence of unfavorable parameters [68]. Width of submucosal invasion less than 4 mm, and depth of submucosal invasion less than 2 mm, in the absence of unfavorable parameters, identify tumors with very little risk for nodal involvement, and metastatic capability close to zero per cent [68]. Moreover, by estimating the extent of submucosal invasion, it is possible to identify within the low-risk early colorectal cancer, a subgroup of lesions with virtually no risk of nodal metastasis: depth of submucosal invasion less than0.3 mm (sm1), or depth of submucosal invasion less than 2 mm joined at a width of submucosal invasion less than 4 mm with negative budding [54,68].

These pathological parameters define two groups of early colorectal cancer with different risk of nodal and/or local recurrence: low- and high-risk early colorectal cancer. A low-risk early colorectal cancer is defined as being a completely excised Haggitt level 1 to 3 or Kikuchi Sm1 and possibly Sm2 depth of invasion, with no evidence of poorly differentiated

adenocarcinoma or lymphatic or vascular invasion [62] and low-grade tumor budding [54,80]. It is now generally accepted that local excision, by either endoscopic polypectomy or transanal surgery, is adequate treatment for a low-risk early colorectal cancer [62]. A high-risk early colorectal cancer is defined as one that has one or more of the following characteristics: a positive resection margin, a high tumor grade, an Sm3 or possibly an Sm2 depth of invasion, presence of lymphatic or vascular invasion, or a high grade of tumor budding [54,62,80].

Low- and high-risk early colorectal cancers differ, not only with regard to lymph node metastases, but also to distant metastasis and mortality rates [71]. Such adverse clinical outcomes occur despite the majority of high-risk patients undergoing surgical resection. This observation strengthens the usefulness of this classification not only for addressing the therapeutic choice, but also as a staging procedure.



Width and depth of submucosal invasion. Modified from [68] with permission from Elsevier

REPORTING MALIGNANT POLYPS GROSS FEATURES

- Macroscopic growth pattern: pedunculated/sessile/ flat polyp.
- Greatest dimension.

HISTOLOGICAL FEATURES

- Grade of adenocarcinoma: low-grade/high-grade dysplasia.
- Status of the resection margin.
- Presence or absence of lymphatic or venous invasion.
- Tumoral budding.
- Microstaging:
  - volume of adenoma replaced by the carcinoma;
  - levels of invasion of the submucosa:

- Haggitt's levels (pedunculated polyp)
- Kikuchi's classification (sessile polyp)
- depth and width of infiltration of the submucosa.

PSEUDOCARCINOMATOUS ENTRAPMENT (PSEUDOINVASION)

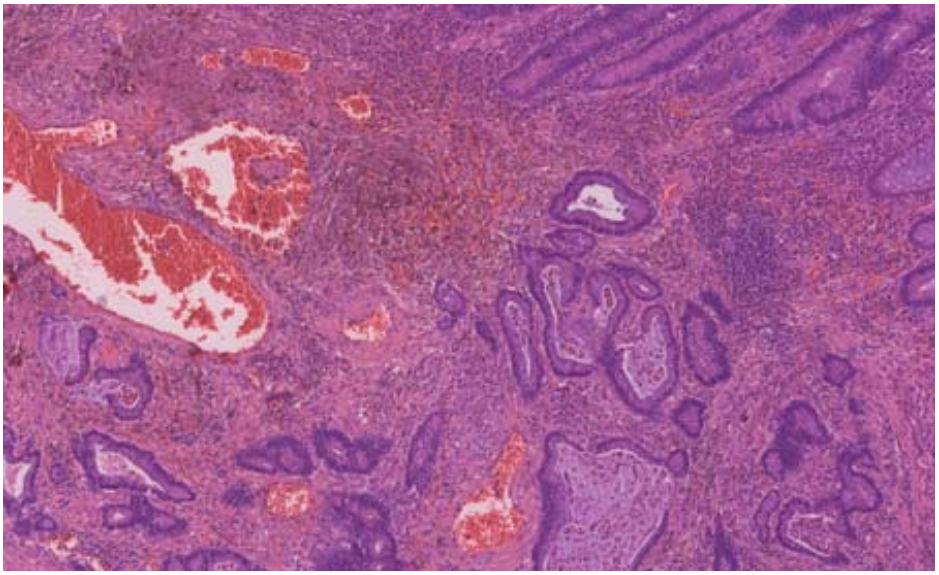
A recognized histological pitfall in diagnosing adenoma is the presence of "entrapped" (pseudoinvasive) dysplastic glands in the submucosa mimicking invasive adenocarcinoma.

Pseudocarcinomatous entrapment, variously termed colitis cystica profunda, submucosal cysts, pseudocarcinomatous invasion, or epithelial misplacement, affects a small proportion of pedunculated adenomas usually located in the sigmoid colon (64% to 85%) [8].

Repeated episodes of torsion lead to hemorrhage, inflammation, and ulceration of the adenoma. As a result, the adenomatous glands herniate through the muscularis mucosae into the underlying submucosa. Forceps biopsies may also cause epithelial displacement: the adenomatous tissue may be pulled further into the stalk by contraction of fibrous tissue as the biopsy site heals [86].

Histologically, areas of pseudoinvasion can be recognized by the presence of adenomatous glands in a submucosa without cytological evidence of malignancy. Pseudoinvasion is

characterized by the presence of entrapped adenomatous glands in a submucosa surrounded by normal lamina propria with hemosiderin deposits, as opposed to a desmoplastic response in invasive carcinoma. The degree of dysplasia in the displaced glands often resembles that of the glands immediately overlying it, and the displaced glands may also coexist with non-neoplastic glands that were displaced along with the neoplastic ones.



Adenoma with pseudocarcinomatous entrapment: at high magnification the displaced pseudoinvasive glands demonstrated low-grade dysplasia and are surrounded by lamina propria. Siderogenous desmoplasia is present within the submucosa (brownish color comes from the presence of hemosiderinladen macrophages)

GROSS EXAMINATION AND CUTTING OF POLYPS

Fixation

Adenomas should be fixed prior to cutting. The polyp should be placed in an adequate volume of fixative (at least ten times the volume of the tissue). The length of time needed for adequate fixation varies with the size of the polyp (i.e. larger polyps need longer fixation). The pathologist can often appreciate when the tissue is adequately fixed and firm enough for subsequent sectioning, by careful palpation of the polyp [9].

Ideally, the endoscopist should indicate the stalk of larger adenomas by placing a needle at its base when the polyp is removed from the endoscope. Realistically,this almost never happens. Occasionally, the pathologist and the endoscopist disagree as to whether a stalk is present or how long the stalk is, since the stalk often retracts into the head of the adenoma. Occasionally, the precise orientation of the polyp cannot be identified clearly; sectioning at several levels may then be needed to recognize the exact anatomical relationships. However, some specimens defy accurate orientation so that the assessment of margins may be impossible. In this case, the margins are reported as not evaluable.

Sampling

Once fixed, the entire lesion should be examined histologically. When one receives polyp biopsies or polypectomy specimens, it is important to record all of the pathological features, including the number of tissue fragments received, their size, their gross morphology (i.e. pedunculated or sessile), and their locations. The stalk of a pedunculated polyp or the point of transection of sessile or semipedunculated polyps should be identified. In sessile and semipedunculated polyps, the point of transection can often be identified as an ashen white area of discoloration. It is possible to identify the excision edge of the specimen due to the presence of a prominent cautery effect [62].

The endoscopist should identify the point of transaction with India ink; a pin is another method of identifying the point of transection in sessile polyps [9]. Polyps should be cut in the sagittal plane through the stalk or the point of transection, such that all the relevant microscopic landmarks will be easily assessable. If piecemeal polypectomy is unavoidable, the endoscopist can place the true transected margin in a separately identified container, or use a pin or India ink to identify the true margin of transection. It is also important that the endoscopist

informs the pathologist whether the polypectomy was believed to be complete or incomplete [9].

Tissue fixation ensures retention of the ball shape, making identification of the resection site difficult. This artifact can be avoided by having the endoscopist place sessile polyps on a firm matrix, such as a piece of paper or Gelfoam, before placing the specimen in the fixative.

If the lesion is pedunculated and received in a fresh state, it can be fixed in such a way that the stalk is pinned to a piece of cork. The histological classification of fractional biopsies of smaller adenomas (<1.7 cm) are in 88.9% agreement with the final diagnosis in the polypectomy specimen, whereas the reliability of the biopsies in accurately diagnosing adenomas >1.7 cm is only 27.68%. Invasive carcinomas are frequently missed in biopsies taken of larger lesions [8].

This diagnosis is made on either a polypectomy specimen or a biopsy of sessile lesions. Diagnosing areas of invasive carcinoma on a midsagittal section of a pedunculated adenoma is often easier than making a diagnosis of invasion on a small forceps biopsy of a larger lesion. Biopsy fragments in which the

neoplastic cells mingle with the fat, medium-sized blood vessels, nerve trunks, ganglia, or large lymphatics can be diagnosed as invasive lesions.

PATHOLOGY OF POST-POLYPECTOMY RESECTION SPECIMENS

The reports from pathologists with regard to the postpolypectomy resection specimens have to focus on two significant statements: (1) the presence of residual neoplastic cells at the site of previous polypectomy, and (2) the presence of lymph-nodal metastases. On gross examination of the resection specimens, it is important to identify the actual polypectomy site. If the resection is performed within approximately 10 days post-polypectomy, the polypectomy site will usually be apparent as an area of erosion, ulcer, or induration. When resections are performed more than 10 days post-polypectomy, it is often difficult to identify the polypectomy site, which has probably healed and re-epithelialized.

In a fresh unfixed specimen, if the polypectomy site is not grossly obvious, the pathologist, by careful palpation, can often find an area of induration that corresponds to the polypectomy site. The polypectomy site should be confirmed microscopically.

In instances of delayed resection with re-epithelialization of the polypectomy site, one should look for focal fibrosis, thrombosed submucosal blood vessels, occasional giant cells, disruption of the muscularis mucosae, etc, to confirm the polypectomy site. If, after taking the routine number of sections, one is unsuccessful in finding the polypectomy site, more random sections should be taken. No specific number is recommended, but the sampling should be extensive. If, after extensive sampling, the site is not found, the pathology report should clearly indicate that the polypectomy site was not found. This should indicate to the surgeon that there is a possibility that the correct area of bowel may not have been removed. To facilitate finding the polypectomy site, the endoscopist might tattoo the area with India ink. This tattoo remains for several months [9].

With respect to lymph nodes, it should be remembered that all nodes present must be sampled. It has been shown that a minimum of 12 to 18 lymph nodes must be examined to accurately predict regional node negativity in colorectal cancer [87–90]; moreover it has been suggested that 12 lymph nodes be considered the minimum number that is acceptable [72,88].

MATERIALS AND METHODS

The centre of study was Department of Medical Gastroenterology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3.

STUDY DESIGN

Prospective

VENUE

Rajiv Gandhi Government General Hospital, Chennai-3.

DURATION OF STUDY

December 2008 to January 2011.

COLLABORATING DEPARTMENT

Department of Pathology, Madras Medical College, Chennai-600 003.

METHODOLOGY

Patients who are attending department of Medical Gastroenterology and those patients referred from other medical and surgical wards. Patients suspicious of gastroenterology polyps or with family history of polyps.

PATIENT SELECTION

Inclusion Criteria

Patients with family history of GI polyps and those found to have GI polyps on routine endoscopy.

Exclusion Criteria

1) Patients not willing for consent
2) Patients with serious cardiac and respiratory disorders
3) Pregnant women
4) Respiratory failure
5) Renal failure
6) Psychiatric diseases

PROTOCOL

1) All the patients who met the above criteria were included in the study and got admitted in our department.
2) The following were noted in each patient.
    a. Age
    b. Sex
    c. Educational Status
    d. Symptoms of patients suspicious of GI polyps

3) Data collection methods

a. Detailed clinical history

b. Hemogram

c. Upper and lower GI endoscopy as applicable

d. Biopsy of the lesion

e. Biopsy of the specimen to be sent for histopathologic examination.

RESULTS

Total number of patients – 50

Total number of male patients – 33

Total number of female patients – 17

Male : Female ratio – 2:1

AGE

Mean age

Male patients – 55.6 years

Female patients – 49.1 years

UPPER GI FINDINGS

Esophageal polyps – 4 (8%)

Gastric polyps – 14 (28%)

Duodenal polyps – 4 (8%)

Colonic polyps – 28 (56%)

CLINICAL PRESENTATION

Esophageal polyps presented with dysphagia-1, Odynophagia-1, Hold up -2.

GASTRIC POLYPS

7 patients (50%) presented with non specific symptoms like pain abdomen. 4 patients presented with features of dyspepsia like belching, abdominal bloat. Two patients presented with upper GI bleed. One hematemesis and one patient with melena.

DUODENAL POLYPS

Of the four patients who presented with duodenal polyps one patient presented with vomiting, one patient presented with chronic diarrhea, two patients presented with vague abdominal pain.

COLONIC POLYPS

26 patents presented with bleeding per rectum (95%).

2 patients presented with blood and mucous diarrhea and altered bowel habits.

TYPES OF POLYPS

Sessile polyps	:	25 (50%)
Pedunculated polyps	:	8 (10%)
Polypoidal mass	:	16 (32%)
Pseudo polyp	:	1 (2%)

HISTOPATHOLOGY

Inflammatory polyps	:	11 (22%)
Hyperplastic polyps	:	18 (36%)
Tubular Adenoma	:	8 (16%)
Villous Adenoma	:	2 (4%)
Tubulo Villous	:	5 (10%)
Adeno carcinoma (Gastric)	:	1 (2%)
Adeno carcinoma (Colonic)	:	2 (4%)
Lympho proliferative disorder	:	1 (2%)
Fibro epithelial polyp	:	1 (2%)
Peutz Jeghers Polyps	:	1 (2%)

DISCUSSION

Of all the gastro intestinal polyps in our study colonic polyps was predominant – 28 patients (56%).

Symptom wise

Bleeding per rectum	: 14
Altered bowel habits	: 4
Pain during defecation	: 4
Chronic diarrhea	: 2
Perianal fistula with serous discharge	: 1
One patient had been operated for growth rectum 4 months earlier	: 1
Iron deficiency anemia	: 1
Perioral pigmentation S/o Peutz Jeghers	: 1

From the above analysis it is clear that bleeding/ rectum and altered bowel habits were the presenting symptoms in majority of patients with colorectal polyps (64%) which is in contrast to a study on colorectal polyps where only 6.04% patients presented with bleeding per rectum, pus discharge and perianal pain.

Ref: A study on gastrointestinal polys- Clinico pathological aspects: Esmaily HA, Mostafapour E, Research Journal of Biological Sciences – 57-63-2008.

COLONIC POLYPS- HISTOPATHOLOGY

Tubular adenoma	:	5
Tubulo villous adenoma	:	5
Villous adenoma	:	3
Hyperplastic polyps	:	10
Adeno carcinoma	:	3
Peutz – Jeghers Polyp	:	1
Pseudo Polyp	:	1

It is clear from the above data that hyperplastic polyps are the most common (35%) histologic type. This is in contrast to a study by

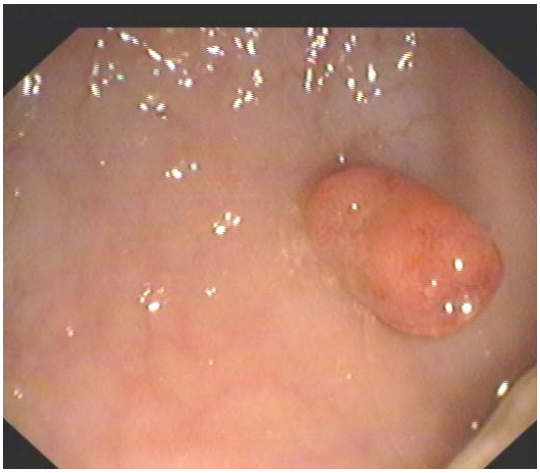
Esmaeily HA, Mostafapour E: Gastro intestinal polyps- Clinicopatholoigcal aspects- Research Journal of Biological Sciences, 57-63, 2008.

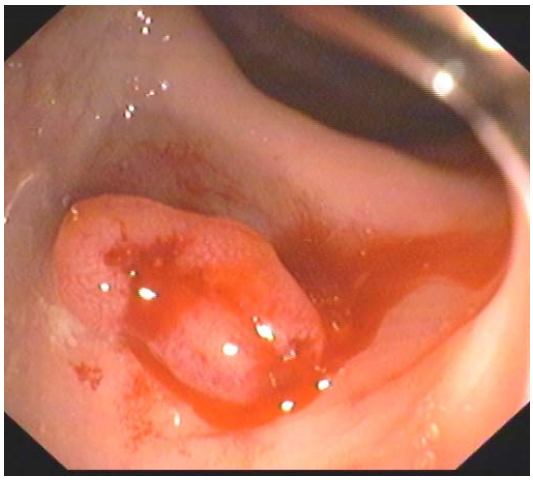
Where tubularadenoma was the frequent subtype constituting 71% of all adenomatous polyps.

One patient who had perioral pigmentation and suspected of having Peutz Jeghers syndrome was evaluated. When the patient was undergoing CT enteroclysis developed signs of intestinal obstruction. Patient was operated and two polyps retrieved from jejunum. Histopathology of the polyps showed features of Peutz Jegher's Polyp.

One patient who presented with blood and mucous diarrhea showed endoscopic features of inflammatory bowel disease and histopathology showed inflammatory pseudopolyp. 2 patients had histopathologic features of adenocarcinoma.

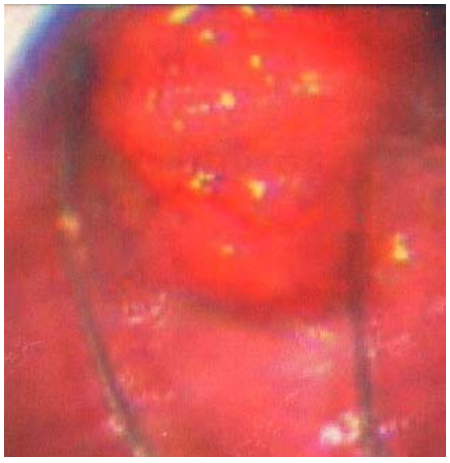
Sigmoid Polyp



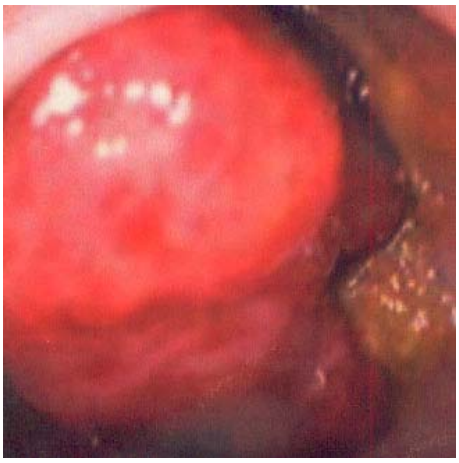


Rectum

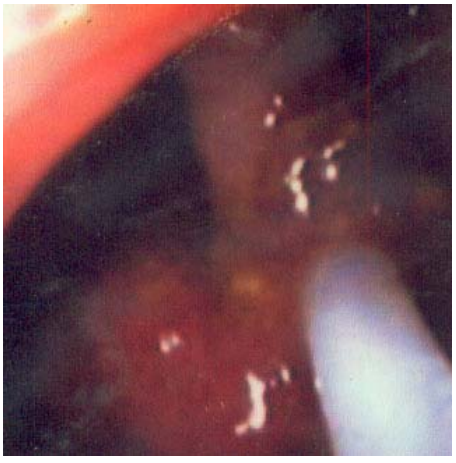
Snare Around Polyp



Recto- Sigmoid



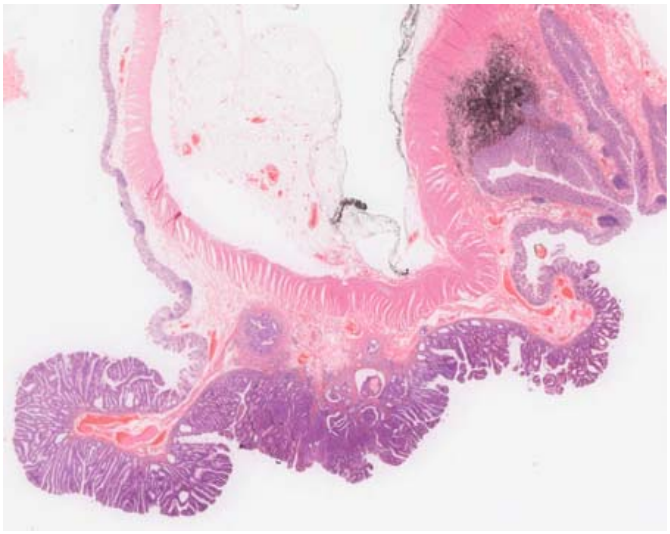
Stalk of the polyp



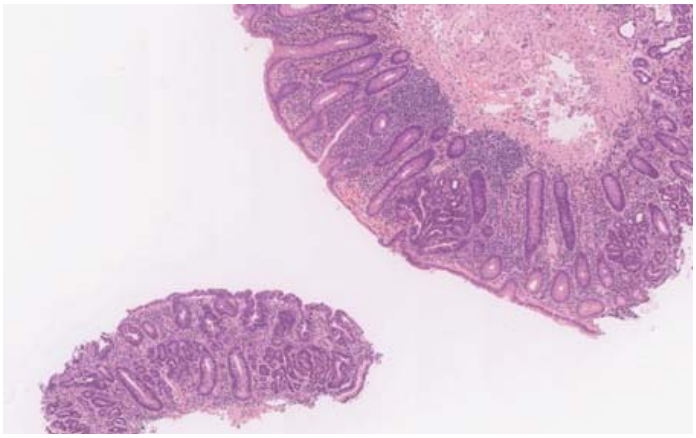
Retrieved Polyp

HISTOPATHOLOGY OF POLYPS

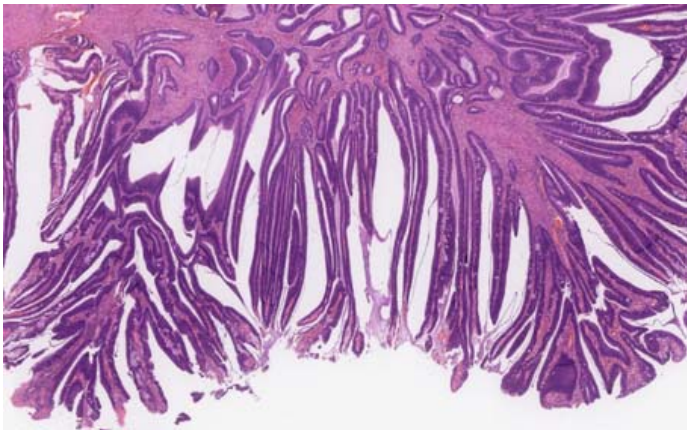
Pedunculated polyp



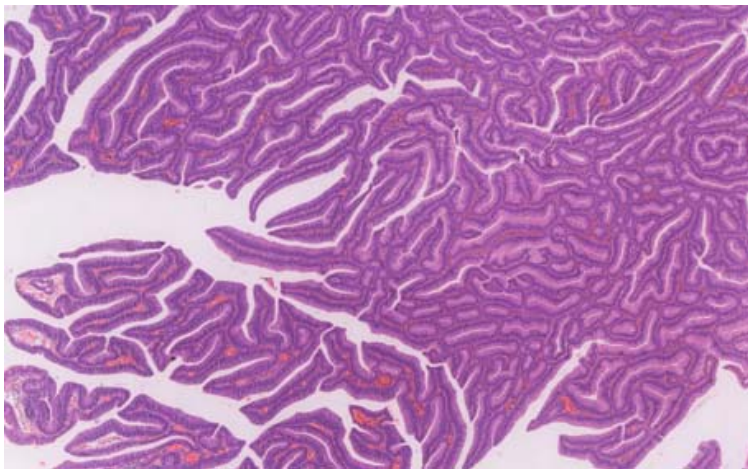
Sessile polyp



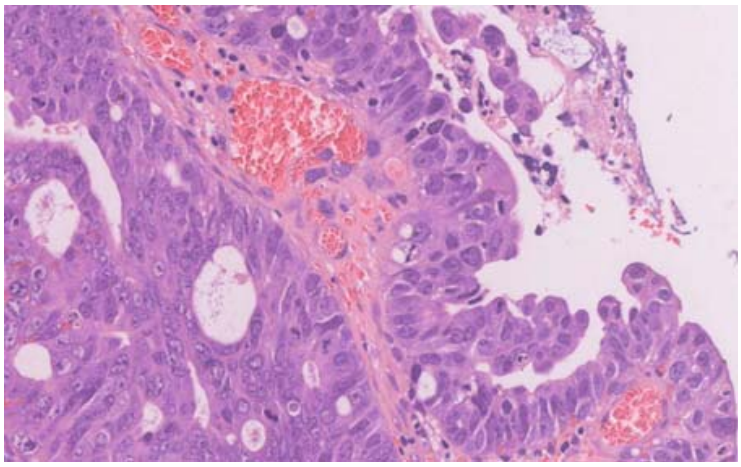
Flat adenoma



Villous adenoma



Tubulo-villous adenoma



High-grade dysplasia

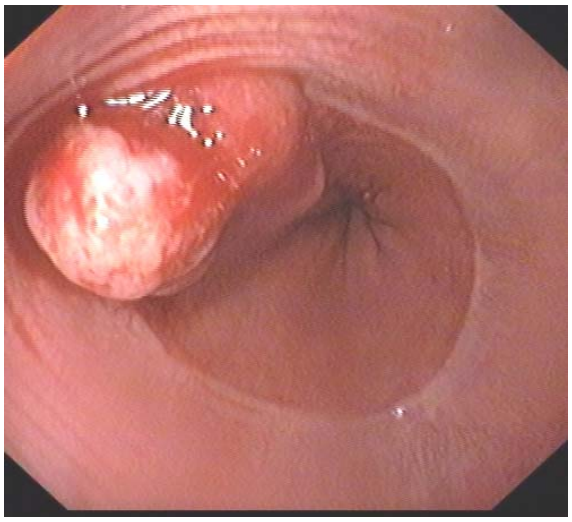
ESOPHAGEAL POLYPS

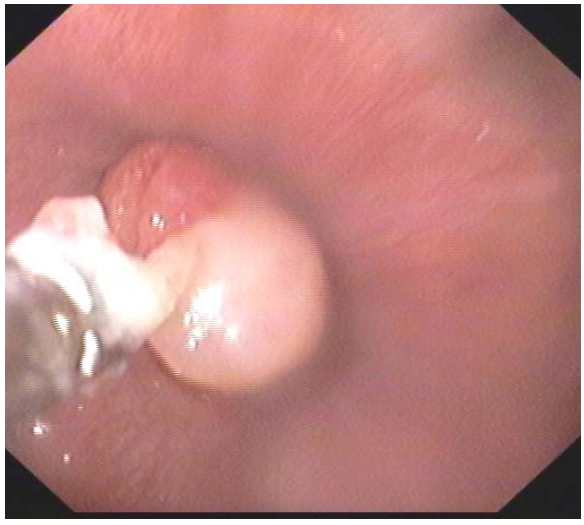
Esophageal polyps in this study showed histopathologic features showed histopathologic features of hyperplastic polyps – 2 (50%), Inflammatory polyps-1.

This is similar to a study on hyperplastic polyps of the esophagus and esophago gastric junction.

Histologic and clinico pathologic findings.

Abraham SC, Yardley JH, Johns Hokins University school of Medicine, Baltimore.





GASTRIC POLYPS

Gastric polyps in our study presented with the following symptoms

- Hemetesis- 1
- Melena-1
- Dyspeptic symptoms-6
- Vomiting-3
- Anaemia for evaluation- 2
- Asymptomatic -1

As for the location of gastric polyps only 2 patients showed fundic polyps, antral polyps were 5, polyps in pyloric region 4, polyps involving body 1, 2 patients showed polyps scattered throughout the stomach.

The histopathology of one patient with antral polyp turned out to be **adenocarcinoma**. Fundic gland polyps were inflammatory polyps (3). Rest of the gastric polyps were hyperplastic (3). adenomatous polyps (2).

GASTRIC POLYPS (CARDIA)

DUODENAL POLYPS

In the duodenal polyps in our study one turned out be a lympho proliferative disorder (IPSID) confirmed with immuno histochemistry. Three others showed non specific inflammation (75%).

In a study by

Remmelew Hartmannw, Vonder Ladden on duodenal polyps reported in histopathology of duodenal polyps in pubmed" Hyperplastic polyps were most common (68%).

Another Study,

Prospective study of prevalence endoscopic and histopathologic characteristics of duodenal polyps in patients submitted to endoscopy

Jepsen JM, Person M, Jakobsen O, Institute of Pathology/ University of Arthus, Denmark, Scand J of GE 1994, 29: 483.

Histopathology of duodenal polyps is inconsistent. In the descending duodenum polyps are rare but significant number of them are adenomas. Biopsy is therefore mandatory in this localization.

CONCLUSION

This study has highlighted the importance of screening for patients with upper Gastro Intestinal Symptoms by detection of unsuspected polyps (44% upper GI polyps). Regarding lower gastrointestinal polyps colonoscopic screening has helped to detect polyps and the histopathological types has helped us in offering proper management options like polypectomy is many. In two patients which appeared as non malignant histopathological examination detected malignancy in them and further investigations helped us to offer curative resections for these patients.

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MASTER CHART

S.No	Name	Age	Sex	Clinical Features	Endoscopic Findings	Histopathology
1.	Chinnaponnu	45	F	Asymptomatic	Upper GI endoscopy: Sessile polyp in the antrum nodular thickened mucosa	Infiltrating adenocarcinoma-Poorly differentiated
2.	Latha	42	F	Vague abdomen pain vomiting on and off	Bx from sessible polyp in the bulb	Superficial ulceration of mucosa with inflammation cell infiltration of lamina propria
3.	Muthalagan	60	M	Occassional hold up of solids	Bx from small polyp above OGJ	Shows a tiny polypoidal tissue covered by columnar epithelium with goblet cells inflammatory cells in the stroma. Imp: Inflammatory polyp
4.	Anthonysmay	58	M	Bleeding perrectum	Colonoscopy findings. A small sessile polyp at 60 cms	Shows tubules and glands of varying sizes lined by single layer of columnar epithelium. Imp: Tubular adenoma, No c/o dysplasia
5.	Anantah Sayanam	40	M	Bleeding per rectum altered bowel habits	Colonoscopy findings polyps of varying sizes from mucosa of rectum both sessile and pedunculated polyps	Shows mucosa of surface lined by several villous process lined by single layer of columnar cells shows some tubular glands in the mucosa and submucosa. Imp:Tubulovillous adenoma

S.No	Name	Age	Sex	Clinical Features	Endoscopic Findings	Histopathology
6.	Sivasamy	60	M	Bleeding per rectum	Sessible polyp seen in rectum (Bx taken)	Shows a polypoidal mass composed of tubular glands of varying sizes lined by single layer of columnar epithelium with few papillary process
7.	Munawar Ahamed	20	M	Chronic diarrhea	Bx from polypidal lesion in D2. ? Lymphoma, ? Lymphangiectasia	Shows flo lymphoproliferative. To confirm with IHC markers
8.	Subramani	59	M	Vague abdomen discomfort	Bx from polypoidal lesion in bulb	Shows superficial ulceration of duodenal mucosa with lymphocytic and on sunplulic infiltration no e/o malignancy
9.	Veerammal	37	F	Altered bowel habits	Colonoscopy: Pedunculated polyp seen at proximal transverse colon (Bx taken)	Features S/o infiltrating adenocarcinoma
10.	Jayaseeli	60	F	Vague abdomen discomfort	OGD: Polypoid lesion seen at prepyloric region	Shows hyperplastic polyp with C/o. congestion and mild inflammation
11.	Ranganathan	71	M	Bleeding per rectum	Colonoscopy: Sessile polyp in rectum. Multiple diverticulae in cecum and ascending colon	Shows fragments of hyperplastic colonic mucosa with one showing F/o. tubular adenoma and villous process. Imp: Tubulo villous adenoma.

S.No	Name	Age	Sex	Clinical Features	Endoscopic Findings	Histopathology
12.	Kuttiammal	62	F	Pain abdomen passes black tarry stools	OGD: multiple polyps in stomach involving body lesser and grater curve (Bx taken)	Shows fragments of hyperplastic gastric mucosa with superficial ulceration nnappanand inflammatory cell infiltration. Imp: Hyperplastic polyp with ulceration.
13.	Chinnappan	73	M	Vague abdomen discomfort	Sessile polyp in distal antrum	Hyperplastic polip
14.	Marimuthu	70	M	Pain during defecation occasional bleeding PR	Coloscopy: passed upto 50cm from analverge small pedunculated polyp at 18cm (Bx A) multiple small sessile polyps seen between 7-12cms from anal verge (Bx)	Both biopsy fragments showed features of hyperplastic polyp
15.	Balakrishnan	48	M	Pain abdomen and one episode of hematemesis	OGD: Multiple small polyps scattered throughout the stomach	Shows fragments of hyperplastic polyps
16.	Jayanhthi	22	F	Bleeding per rectum	Colonoscopy: Multiple polyps involving entire colon	Villous adenoma with low grade dysplasia
17.	Shankar	61	M	Pain during defecation	Anorectal polypectomy specimen	Section shows polypoid lesion showing surface and necrotic acute inflammatory granulation tissue. IHC:CD34-Neg, CD 20-Positive

S.No	Name	Age	Sex	Clinical Features	Endoscopic Findings	Histopathology
18.	Ragupathy	74	M	Pain during defecation	Colonoscopy: Sessile polyp seen just beyond anal verge and normal overlying mucosa	Chronic inflammatory polyp
19.	Shanmugam	59	M	Altered bowel habits	Colonoscopy: Passed upto 5cm of terminal ileum tiny polyp seen at cecum	Colonic mucosal glands with predominantly normal mucin with some glands showing low grade dyslasia. Imp:Adenoma
20.	Chandra	55	F	Dyspeptic Symptoms	Sessile polyp in fundus	Non specific inflammation
21.	Doss	44	M	Altered bowel habits with occasional bleeding per rectum	Colonoscopy: Pedunculated polyp visualized in mid descending colon	Features S/o. adenocarcinoma
22.	Yuvarani	33	F	Pain abdomen and dyspepsia	Tiny polyp in the proximal antrum	Non specific inflammatory polyp
23.	Suseela	63	F	Bleeding per rectum	Colonoscopy: Pedunculated polyp with 2cm stalk seen at mid descending colon	Adenomatous polyp
24.	Varatharajan	75	M	Pain abdomen with occasional vomiting	Pedunculated polyp seen at pylorus with a short pedicle	Hyperplastic polyp

S.No	Name	Age	Sex	Clinical Features	Endoscopic Findings	Histopathology
25.	Govindammal	40	F	Dyspeptic symptoms otherwise asymptomatic	Small sessile polyp seen at the junction of body and antrum	Adenomatous polyp with foci shows mild atypia
26.	Ekambaram	55	M	Bleeding per rectum	Colonoscopy: Single pedunculated polyp in sigmoid colon. Polypectomy done	Features of tubular adenoma adjacent mucosa shows inflammation and mild polypoidal hyperplasia
27.	Bhuvaneswari	25	F	Blood and mucous diarrhoea	Colonoscopy: Colonic mucosa inflamed with ulceration and loss of vascular pattern multiple polyps of varying seen 50cm from anal verge	Markedly inflamed colonic mucosa with features of ulcerative colitis and hyperplastic pseudopolyp
28.	Jeeva	60	F	Pain abdomen and dyspepsia	Bx taken from Gastric antrum	Fragments of polypoidal mucosa with benign cytology
29.	Ramasamy	48	M	Chronic diarrhea and occasional bleeding per rectum	Colonoscopy: Scope passed upto cecum Bx taken from sessile polyp in ascending colon	Features of tubular adenoma
30.	Periyanayaki	70	F	Late onset dyspepsia	OGD: Multiple polyps in antrum, fundus and leser curve	Hyperplastic polyp with C/o mild and inflammation
31.	Gnanprakasam	58	M	Perianal fistula and serous discharge	Colonoscopy: Rt. Small sessile polyps of size 4mm another polyp 2mm seen 35cm from anal verge	Features of tubular adenoma

S.No	Name	Age	Sex	Clinical Features	Endoscopic Findings	Histopathology
32.	Kalidoss	50	M	Vague abdomen discomfort and looze stools 2 months	2 sessile polyps in cecum	Hyperplastic polyp
33.	Govindasamy	70	M	Growth rectum (low anterior resection done)	Colonoscopy: Small sessile polyp 25cm from anal verge	Features of hyperplastic polyp
34.	Sukumaran	62	M	Altered bowel habits/ constipation alternating with diarrhea	Colonoscopy: Polyp in ascending colon	Hyperplastic polyp
35.	Pattu	70	F	Peptic ulcer like symptomus	Sessile polyp in 1st part of duodenum	Hyperplastic polyp
36.	Durairaj	63	M	Occassional hold up	Small esophageal polyp 27cm from the incisor teeth	Hyperplastic squamous epithelium without e/o malignancy
37.	Pandiyan	61	M	Chronic constipation	Colonoscopy: A small polyp seen at splenic flexure	Shows small polypoidal mass composed of glands lined by mucous epithelium. Imp: Hyperplaatic polyp
38.	Sankaran	56	M	Bleeding per rectum	2 sessile polyps seen at 10cm from anal verge	Shows strips of rectal mucosa with c/o non specific inflammation
39.	Angaiah	68	M	Odynophagia and holdup	Polyp at OGJ	Hyperplastic polyp
40.	Sundaram	62	M	Iron deficiency anemia	Colonoscopy: Small sessile polyp in ascending colon	Hyperplastic polyp

S.No	Name	Age	Sex	Clinical Features	Endoscopic Findings	Histopathology
41.	Moorthy	54	M	Blood and mucous diarrohea	Pedunculated polyp in sigmoid colon (Bx taken)	Section shows fragments of polypoidal mass containing tubular glands with one focus showing small villous process with mild dysplastic changes. Imp: Tubulo villous adenoma with dysplastic change
42.	Mallika	47	F	Occassional vomiting	Bx from polyp in the pyloric ring	Hyperplastic polyp
43.	Dasarathan	66	M	Bleeding per rectum	Colonoscopy: 2 polyps sessile and pedunculated seen in rectum and about 18cm from anal verge	Tubulo adenomatous changes seen
44.		50	F	Pain and bleeding during defecation	Colonoscopy: Sessile polyp seen in rectum	Hyperplastic polyp
45.	Eswaran	30	M	Blood and mucous stools	Multiple polyps throughout the colon ?FAP	Section shows a polyp compsed of glands arranged in tubular pattern, and in villous patter lined by columnar epithelial cells having uniform bowel muclei. Imp: Tubulovillous adenoma
46.	Murugan	20	M	Peroral pigmentation of palms suspected Peutz Jeghers syndrome	Rectal polyp	Adenomatous polyp

S.No	Name	Age	Sex	Clinical Features	Endoscopic Findings	Histopathology
47.	Shankar	35	M	Patient presented with features of intestinal obstruction. Patient also had perioral pigmentation	Surgically removed polyp from jejunum	Peutz jeghers polyp
48.	Selvam	40	M	Patient presented with dysphagia	3mm sessile polyp at 32 cm from incisor teeth (esophageal polyp)	Fibro epithelial polyp
49.	Shanmugam	65	M	Bleeding for rectum	Colonoscopy: Scope passed upto spelenic flexure 5mm polyp in recto sigmoid	Shows small polypoidal mass composed of tubular glands lined by columnar epithelial cells. Imp: Tubular adenoma
50.	Vanitha	45	F	Anaemia for evaluation	OGD: Large polypoidal lesion in the prepyloric region abutting the pyloric opening	Shows fragments of antral mucosa with hyperplastic glands and non specific inflammation. Imp: Hyperplastic polyp.

INFORMED CONSENT FORM

Title : Incidence and Prevalence of Gastrointestinal Polyps - A clinical, endoscopic and histopathologic correlation.

Name of the Participant :

Name of the Investigator : Dr.Kani Shaikh Muhammad

Name of the Institution : Madras Medical College

Documentation of the informed consent

I _____ have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered.

I am over 18 years of age exercising my free power of choice, I heareby give my consent to be included as a participant in Incidence and Prevalence of Gastrointestinal Polyps - A clinical, endoscopic and histopathologic correlation.

1) I have read and understood this consent form and the information provided to me.

2) I have had the consent document explained to me.

3) I have been explained about the nature of the study.

4) I have been explained about my rights and responsibilities by the investigator.

5) I have been adviced about the risk associated with my participation in this study.

6) I agree to Co-operate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.

7) I have not participated in any research study with in the past _____ month(s).

8) I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.

9) I am also aware that the investigator may terminate my participation in the study at any time, for any reason without my consent.

10) I hereby give permission to the investigators to release the information obtained from me as a result of participation in this study to the sponsors, regulatory anthorities Govt. agencies and IEC, I understand that they are publicly presented.

11) I understand that my identity will be kept confidential if my data are publicly presented.

12) I have had my questions answered to my satisfaction.

13) I have decided to be on the research study.

I am aware that if have any question during this study. I should contact the investigator. By signing this consent form I atleast that the information given in this document has been clearly explained to me and understood by me. I will be given a copy of this consent document.

For adult participants

Name and signature / Thumb impression of the participant

Name _____ Signature _____

Date _____

Address and contact number of the impartial witness

Name and signature of the investigator or his representative obtaining consent:

Name _____ Signature _____

Date _____

ஆராய்ச்சி ஒப்புதல் கடிதம்

ஆராய்ச்சி தலைப்பு

பெயர்	:	தேதி	:
வயது	:	உள் நோயாளி எண்	:
பால்	:	ஆராய்ச்சி சேர்க்கை எண்	:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு விளக்கப்பட்டன.

எனக்கு விளக்கப்பட்ட விஷயங்களைப் புரிந்து கொண்டு நான் எனது சம்மதத்ததை தெரிவிக்கிறேன்.

எனக்கு வயிறு மற்றும் குடல் கட்டிகளிலிருந்து திசுக்களை எடுத்து பரிசோதனை செய்து கொள்ள சம்மதம்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின்பேரில்தான் பங்கு பெறுகிறேன் மற்றும் நான் இந்த ஆராய்ச்சியிலிருந்து எந்நேரமும் பின்வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் புரிந்து கொண்டேன்.

நான் வயிறு மற்றும் குடல் கட்டிகள் குறித்த இந்த ஆராய்ச்சியின் விவரங்களைக் கொண்ட தகவல் தாளைப் பெற்றுக் கொண்டேன்.

எனக்கு அறுவைச்சிகிச்சை செய்யப்பட்டு நோய்க் குறியியல் துறையில் சதைப் பரிசோதனைக்கு பயன்பட்ட மெழுகுக்கட்டிகளை வைத்து ஆராய்ச்சி மற்றும் சிறப்புப் பரிசோதனை செய்து கொள்ள சம்மதம் தெரிவிக்கிறேன்.

சதை பரிசோதனை செய்வதற்கு முன் வலி தெரியாமல் இருப்பதற்காக ஊசி (லிக்னொகெய்ன் இஞ்செக்ஷன்) போடுவதற்கும் சம்மதிக்கிறேன். மேற்கண்ட ஊசி போடுவதற்கு முன் ஒவ்வாமை (அலெர்ஜி) பரிசோதிக்க மேற்கண்ட ஊசியை தோலில் போட்டுக் கொள்ளவும் சம்மதிக்கிறேன்.

மேற்கண்ட ஊசியை போடும் போதோ அல்லது சதை பரிசோதனை செய்யும் போதோ ஏதேனும் பின் விளைவுகள் (அரிப்பு, தோல் வீக்கம், மயக்கம், தலைச்சுற்றல், வாந்தி முதலியன) ஏற்படலாம் என மருத்துவர் மூலம் தெரிந்துக் கொண்டேன்.

கையொப்பம்

ஆராய்ச்சி தகவல் தாள்

தங்களது அறுவை சிகிச்சையின் போது எடுக்கப்பட்ட கட்டிகளிலிருந்து திசுக்கள் இங்கு பரிசோதனைக்கு பெற்றுக் கொள்ளப்பட்டது.

சென்னை அரசு பொது மருத்துவமனைக்கு வரும் நோயாளிகளிடம் இருக்கும் வயிறு மற்றும் குடல் கட்டிகளைப் பற்றிய ஆராய்ச்சி இங்கு நடைபெற்று வருகின்றது.

வயிறு மற்றும் குடல் உறுப்புகளில் தோன்றும் கட்டிகள் பல வகையானவை. அவற்றில் சில கட்டிகள் புற்றுநோயாக மாறுவதற்கு வாய்ப்புகள் அதிகம் உண்டு. சென்னை பொது மருத்துவமனைக்கு வரும் நோயாளிகளிடம் எவ்வித குடல் கட்டிகள் தோன்றுகின்றன என்பதையும், அவை புற்று நோயாக மாறும் தன்மை பற்றியும் அறிந்து கொள்வதே இந்த ஆராய்ச்சியின் நோக்கமாகும்.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். இந்த ஆராய்ச்சியில் உங்களுடைய திசுக்களை எடுத்து சில சிறப்புப் பரிசோதனைக்கு உட்படுத்தி அதன் தகவல்களை ஆராய்வோம். அதனால் தங்களது நோயின் ஆய்வறிக்கையோ அல்லது சிகிச்சையோ பாதிப்புக்கு ஏற்படாது என்பதையும் தெரிவித்துக் கொள்கிறோம்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின் வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த சிறப்புப் பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின்போது அல்லது ஆராய்ச்சியின் முடிவின்போது தங்களுக்கு அறிவிக்கப்படும் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் **பங்கேற்பாளர் கையொப்பம்**

தேதி

CERTIFICATE OF APPROVAL

To

Dr. Kani Shaikh Muhammad
PG in DM Gastroenterology
Madras Medical College, Chennai -3.

Dear Dr. Kani Shaik Muhammad

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled " Incidence and Prevalence of Gastrointestinal Polyps – a clinical, endoscopic and histopathologic correlation" No. 08022011.

The following members of Ethics Committee were present in the meeting held on 17.02.2011 conducted at Madras Medical College, Chennai -3.

1.	Prof. S.K. Rajan, MD	– Chairperson
2.	Prof. A. Sundaram, MD Dean i/c , Madras Medical College, Chennai -3	– Member Secretary
3.	Prof R. Sathianathan Director , Institute of Psychiatry, MMC,Ch-3	– Member
4.	Prof R. Nandhini, MD Director, Institute of Pharmacology, MMC, Ch-3	– Member
5.	Prof. Pregna B. Dolia MD Director , Institute of Biochemistry, MMC, Ch-3	– Member
6.	Prof. C. Rajendiran .MD Director , Institute of Internal Medicine, MMC, Ch-3	– Member
7.	Prof. Geetha Subramanian, MD,DM Prof. & Head , Dept. of Cardiology, MMC, Ch-3	– Member
8.	Thiru. A. Ulaganathan Administrative Officer, MMC, Chennai -3	– Layperson
9.	Thiru. S. Govindasamy . BA.BL	– Lawyer
10.	Tmt. Arnold Soulina	– Social Scientist

We approve the proposal to be conducted in its presented form.

Sd /. Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report

Member Secretary, Ethics Committee